APPENDIX A

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

No. 03-5020

JULIAN M. WHITAKER, *et al.*,
Appellants,

v.

TOMMY G. THOMPSON, Secretary, U.S. Department of Health and Human Services, *et al.*,
Appellees.

Appeal from the United States District Court [*]
for the District of Columbia
(No. 99cv03247)

Argued November 10, 2003 Decided January 9, 2004

Before: RANDOLPH and ROBERTS, *Circuit Judges*, and WILLIAMS, *Senior Circuit Judge*.

Opinion for the Court filed by Senior Circuit Judge WILLIAMS.

WILLIAMS, *Senior Circuit Judge*: When substances aimed at the treatment or prevention of disease are marketed, their regulation by the Food and Drug Administration ("FDA") commonly turns on the nature of the claims made about the substance. Items to be sold with "drug claims," including foods and dietary supplements, are subject to ex-

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[*] Bills of costs must be filed within 14 days after entry of judgment. The court looks with disfavor upon motions to file bills of costs out of time.

tensive testing; foods or dietary supplements that merely make "health claims" pass muster far more easily. This case turns primarily on whether the FDA faithfully applied the Federal Food, Drug and Cosmetic Act ("FFDCA"), 21 U.S.C. § 301 *et seq.*, in its analysis of a petition by Dr. Julian Whitaker and others (for simplicity's sake, "Whitaker") to approve their intended marketing of "saw palmetto," an extract from the pulp and seed of the dwarf American palm, *Serenoa repens*, under a label that they argued was a "health claim."

Whitaker proposed a label stating: "Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)." Petition, May 25, 1999, p. 18. BPH is a non-cancerous enlargement of the prostate that affects almost half of men over 50. The FDA denied the petition. In explaining the decision, it drew a distinction between claims regarding use of a product to maintain health and to "prevent" disease, on the one hand, and claims that a product could "treat" a disease, on the other. The former could qualify as "health claims," but the latter would always be considered "drug claims." May 26, 2000 FDA Letter ("FDA Letter") at 2, 7-10. As BPH is classified as a disease despite its comparative ubiquity, and the proposed label indicated an intent to treat it, the FDA decided that saw palmetto could not be marketed under that label without approval as a drug. Whitaker challenged the FDA's decision in district court on statutory and First Amendment grounds. The district court granted the FDA's motion to dismiss, *Whitaker v. Thompson*, 239 F. Supp. 2d 43 (D.D.C. 2003), and Whitaker appealed. We affirm.

* * *

The statutory claim

The FFDCA definition of "drug" includes "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease," 21 U.S.C. § 321(g)(1)(B), which

would seem by its plain terms to cover the marketing of a substance intended to mitigate the symptoms associated with BPH. But that apparent simplicity is undermined by language added in 1990 by the Nutrition Labeling and Education Act ("NLEA"), Pub. L. No. 101-535, 104 Stat. 2353, which created a separate procedure authorizing "health claims" for food (or for dietary supplements classified as food). The general purpose of the NLEA appears to have been to allow the dissemination—subject to a regulatory approval process —of certain dietary and health information on food products without requiring that those products be regulated as drugs. Specifically, the NLEA amended the FFDCA to authorize the sale of dietary supplements pursuant to "health claims" that "characterize[ ] the relationship of any nutrient . . . to a disease or health-related condition," *id.* § 343(r)(1)(B), so long as the dietary supplement is "subject to a procedure and standard, respecting the validity of such claim, established by regulation of the Secretary," *id.* § 343(r)(5)(D). Whitaker insists, with some justification, that the label he proposed fits within the plain terms of the "health claim" definition.

Thus, although the consequences of classification as a "drug claim" or a "health claim" are quite substantial, Congress has given definitions that at least partially overlap. And it has given little guidance as to how the FDA should sort out claims that seem to fit both definitions. On the one hand, as the FDA points out, the statutory definition of "dietary supplement" plainly contemplates that dietary supplements may fall under the § 321(g) definition of "drugs": it says that a dietary supplement shall be deemed to be a "food" "[e]xcept for purposes of [§ 321(g)]," which defines "drugs" and "counterfeit drugs." 21 U.S.C. § 321(ff). On the other hand, the last sentence of § 321(g)(1), which defines drugs, explicitly states that a "dietary supplement for which a [health claim under § 343(r)] is made . . . is not a drug . . . solely because the label or the labeling contains such a statement." *Id.* § 321(g)(1). This is the statutory provision most directly

relevant to the relationship between health claims and drug claims, but there are at least three ways it might be read, all of them problematic.

First, the last sentence of § 321(g)(1) might mean that a § 343(r) health claim cannot *by itself* establish that a product is "intended" to cure, mitigate, prevent, or treat disease, but such a statement may be used in conjunction with other evidence to establish such intent. Under this view, a health claim would be relevant but not sufficient to establish that a product is a drug. Though this construction provides a grammatically plausible reading of "solely," it is not pressed by any of the parties; in practice it might not make sense, as a product's label may often be the only readily available evidence of the product's intended use.

Second, the sentence in question might mean that a product for which a "drug claim" is made under § 321(g)(1) is not automatically exempt from drug regulation just because the product label *also* makes a separate health claim under § 343(r). This view, urged by amicus American Herbal Products Association, founders on the broad definition of health claims advanced by Whitaker. Such claims appear coextensive with—or perhaps even broader than—§ 321(g) drug claims. The amicus's own brief demonstrates the problem. The amicus seeks to illustrate its reading of the "solely" language, saying that it means only that "use of an authorized health claim on the label of a dietary supplement (*e.g.*, folate reduces the risk of neural tube defects) does not give a manufacturer blanket immunity to include other claims for the product that would otherwise be classified as drug claims (*e.g.*, folate cures cancer)." But if § 343(r) covers anything that characterizes the "relationship" between a nutrient and a disease, then "folate cures cancer" is just as much a health claim as "folate reduces the risk of neural tube defects." Amicus's interpretation of "solely" is sensible only if there are "drug claims" for foods or dietary supplements that are not also "health claims," but Whitaker's broad interpreta-

tion of health claims, and indeed the literal wording of § 343(r)(1)(B) itself, foreclose that possibility.

Finally, the "solely" language in § 321(g) might mean that while a claim that would qualify as a health claim *may* be considered a drug claim, such a claim is not *necessarily* a drug claim. Under this reading, in other words, the statute allows *some* health claims to be exempted from the drug claim definition; but as this class is not defined, it implicitly leaves the choice to the FDA. This interpretation, urged by the FDA, is plausible, but it too is problematic. The statute on its face supplies no guiding principle for determining which health claims should be exempt, and nowhere else evinces an intent to give the FDA unfettered discretion to make so drastic a choice.

Because we are reviewing an agency's interpretation of the statute it is entrusted to administer, and the agency reached its interpretation after a relatively formal process with public notice and comment, cf. *United States v. Mead Corp.*, 533 U.S. 218, 230-31 (2001) (expressing assumption that Congress "contemplates administrative action with the effect of law when it provides for a relatively formal administrative procedure"), we review under the familiar framework established by *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). We first ask whether, applying the "traditional tools of statutory construction," *id.* at 843 n.9, we can discern "the unambiguously expressed intent of Congress," *id.* at 843. If the statute is ambiguous, then we defer to the agency's interpretation so long as it is reasonable. *Id.* at 843-45.

As the discussion above suggests, we see no basis for finding any "unambiguously expressed intent of Congress." We thus turn to the FDA's rationale for classifying certain types of health claims as drug claims in order to decide whether the FDA's approach is reasonable in light of the statute's structure, history, and purposes.

The FDA gave several reasons for classifying claims regarding cure, mitigation, or treatment of an existing disease ("treatment claims") as drug claims and for exempting only health claims that concern reducing the risk of contracting a disease ("prevention claims"). First, the agency reasoned that the legislative history of the NLEA demonstrated an understanding that the health claim provision was intended for claims of prevention rather than ones of treatment. The agency noted statements in the legislative history indicating that the purpose of the health claims provision was to promote long-term health maintenance and prevention of disease, but found nothing suggesting that legislators enacting this provision contemplated treatment of a person's existing disease with dietary supplements. See FDA Letter at 5-6, citing 136 Cong. Rec. H5843 (statement of Rep. Moakley); 136 Cong. Rec. H12,954 (statement of Rep. Moakley); 136 Cong. Rec. H5843 (statement of Rep. Madigan); 136 Cong. Rec. S16,609 (statement of Sen. Metzenbaum); 136 Cong. Rec. S16,610-11 (statement of Sen. Hatch). Indeed, all the specific examples of "health claims" mentioned in the NLEA's legislative history involved prevention rather than treatment. See *id.* at 5, citing H.R. Rep. No. 101-538 at 8, 20, reprinted in 1990 U.S.C.C.A.N. at 3337, 3350; 136 Cong. Rec. H5841 (statement of intent of changes since bill was reported out of committee); 136 Cong. Rec. H12,953 (statement of House floor managers); 136 Cong. Rec. H5841 (statement of Rep. Waxman); 136 Cong. Rec. H12,954 (statement of Rep. Madigan); 136 Cong. Rec. S16,609 (statement of Sen. Mitchell).

Second, the FDA looked to research mandated by Congress when it adopted the NLEA. At that time Congress instructed the FDA, in adopting regulations to implement § 343(r), to investigate ten specific possible health claims, all of which involved prevention—"reduction of the risk of a chronic disease"—rather than treatment. FDA Letter at 5, citing Pub.

L. No. 101-535, § 3(b)(1)(A)(vi),(x), 104 Stat. 2353, 2361 (1990) (see 21 U.S.C. § 343 note).

Third, the FDA noted that the health claims provision was enacted against a backdrop of longstanding application of drug regulation to foods and dietary supplements that made treatment claims—an assertion Whitaker does not dispute. The agency inferred that Congress meant the "solely" sentence of § 321(g)(1) to preserve this practice. FDA Letter at 6.

Finally, the FDA invoked policy concerns to support a distinction between treatment and prevention claims. It argued that, because the health of diseased populations is particularly vulnerable, greater regulation may be justified for products intended for their consumption. Moreover, it argued that treatment claims for symptoms of a disease might lull people with those symptoms into a "false sense of security," leading them to delay a visit to a doctor that might result, for example, in a diagnosis of prostate cancer rather than BPH. *Id.* at 9. Finally, in a statement looking only at possible benefits of its classification decision (and not any of the possible drawbacks), the FDA said that if products could escape regulation as drugs by qualifying as "dietary supplements" that make treatment claims, the protections of the drug approval system could be undermined and incentives to research a substance's health effects would be diminished. *Id.* at 10.

None of these is a knock-down argument, and we doubt that any of them would be sufficient to overcome a strong textual or structural inference in favor of a different interpretation. Certainly there is nothing in the two statutory definitions that would obviously equate claims of "treatment" with drug claims and of "prevention" with health claims. But given our finding that the statute is ambiguous on the critical question of how to classify a claim that meets the statutory definitions both of a drug claim *and* of a health claim, the

legislative history and statutory context invoked by FDA are enough to render its interpretation reasonable.

Whitaker also attacks the FDA's distinction between prevention and treatment claims as arbitrary and capricious. First, he argues that there is no sharp distinction between "prevention" and "treatment"; the two categories may often overlap. They may, of course, but that does not render the distinction either unworkable or irrational. The existence of dawn and dusk, as has often been said, doesn't make it absurd to distinguish between day and night. Second, Whitaker claims that the FDA failed to explain adequately how it could square its decision not to allow Whitaker's claim that saw palmetto extract alleviates symptoms of BPH with the agency's prior approval of a "health claim" that low-fat diets lower cholesterol. See 21 C.F.R. § 101.75(e)(3). But here the FDA plausibly explains that the reference to the lower cholesterol consequences of low-fat diets merely clarifies the mechanism by which heart disease is prevented; the FDA did not authorize a claim that a low-fat diet could treat hypercholesterolemia. So the cholesterol example doesn't show an irrationality in the FDA's attempted distinction.

Finally, Whitaker urges us to adopt his reading of the statute on the ground that this will enable us to avoid the "grave and doubtful constitutional questions" that the FDA's understanding would entail. *United States ex rel. Attorney General v. Del. & Hudson Co.*, 213 U.S. 366, 408 (1909). It is true that the canon of constitutional avoidance can trump *Chevron*. See *Edward J. DeBartolo Corp. v. Florida Gulf Coast Bldg. & Const. Trades Council*, 485 U.S. 568, 575 (1988); *Chamber of Commerce of the United States v. Federal Election Comm'n*, 69 F.3d 600, 604-05 (D.C. Cir. 1995). But if the avoidance canon were extravagantly applied it would tend, in effect, to expand unnecessarily the scope of constitutional prohibitions. Thus in practice the canon's application requires a comparatively high likelihood of unconstitutionality, or at least some exceptional intricacy of

constitutional doctrine. Compare, e.g., *Rust v. Sullivan*, 500 U.S. 173, 191 (1991) (finding the constitutional question not so "grave and doubtful" as to justify avoidance doctrine); *Republican Nat. Committee v. Federal Election Comm'n*, 76 F.3d 400, 409 (D.C. Cir. 1996) (same), with *Chamber of Commerce*, 69 F.3d at 604-05 (applying avoidance doctrine because agency's interpretation would "preclude[ ] appellants from communicating on political subjects with thousands of persons, heretofore regarded by the Commission as members"). As the discussion below should make clear, here we do not find Whitaker's First Amendment objection so powerful as to require us to abandon or qualify *Chevron* deference.

The constitutional claim

Whitaker argues that the FDA's refusal to allow marketing of saw palmetto extract under the proposed label, which he describes as a true and non-misleading statement about its salutary effects on BPH symptoms, violates the First Amendment's limits on restrictions of commercial speech. Under *Central Hudson Gas & Electric Corp. v. Public Service Commission*, 447 U.S. 557 (1980), commercial speech enjoys First Amendment protection only if it concerns a lawful activity and is not misleading. If the speech in question passes those screens, the government may impose restrictions that advance a "substantial" government interest and are no "more extensive than is necessary to serve that interest." *Id.* at 566.

The district court upheld the FDA's decision under the first step of *Central Hudson*. "Because the FDA determined that the saw palmetto claim was a drug claim for disease treatment, it concluded that the claim was an *unlawful* health claim. . . ." *Whitaker v. Thompson*, 239 F. Supp. 2d at 54. Accordingly, the proposed label constituted speech about unlawful activities. *Id.*

So worded, the analysis appears, as Whitaker points out, completely circular. Because sale pursuant to the claim was "unlawful" under the statute, the speech related to an unlawful activity and enjoyed no First Amendment protection.

But one may recharacterize the analysis in a way that avoids the circularity. Assuming that the government may condition the sale of drugs on passage through the elaborate testing that the statute requires (an assumption that Whitaker doesn't question), the key step is the FFDCA principle that classification of a substance as a "drug" turns on the nature of the claims advanced on its behalf.

That principle, in turn, rests on the idea that claims about a product by its manufacturer and vendors, including product labeling, serve as evidence of the sellers' intent that consumers will purchase and use the product for a particular purpose—and, therefore, as evidence whether the product is or is not a drug. See, e.g., *Action on Smoking and Health v. Harris*, 655 F.2d 236, 239 (D.C. Cir. 1980). The question is whether this use of speech to infer intent, which in turn renders an otherwise permissible act unlawful, is constitutionally valid. In fact, the First Amendment allows "the evidentiary use of speech to establish the elements of a crime or to prove motive or intent." *Wisconsin v. Mitchell*, 508 U.S. 476, 489 (1993) (upholding use of speech to determine that defendant selected battery victim because of his race, for purposes of statutory sentence enhancement). Thus it is constitutionally permissible for the FDA to use speech, in the form of labeling, to infer intent for purposes of determining that Whitaker's proposed sale of saw palmetto extract would constitute the forbidden sale of an unapproved drug.

* * *

The judgment of the district court dismissing plaintiffs' claim is

Affirmed.

APPENDIX B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

[Filed Jan. 3, 2003]

Civil Action
NO. 99-3247 (GK)

JULIAN M. WHITAKER, M.D., *et al.*,
Plaintiffs,

v.

TOMMY G. THOMPSON, Secretary,
Department of Health and Human Services, *et al.*,
Defendants,

MEMORANDUM OPINION

Plaintiffs are individuals and companies with a direct financial interest in dietary supplements containing saw palmetto extract as well as a non-profit therapeutic health organization composed of physician members who sell dietary supplements containing saw palmetto extract.[1] They bring this action against the Food and Drug Administration ("FDA"), Jane E. Henney, Commissioner of the FDA,[2] the Department of Health and Human Services ("HHS"), Tommy G. Thompson, Secretary of the HHS, and the United

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[1] Plaintiffs are Julian M. Whitaker, M.D., Pure Encapsulations, Inc., Durk Pearson, Sandy Shaw, and the American Association for Health Freedom (previously known as the American Preventive Medical Association).

[2] While the FDA Commissioner's post is now vacant, Jane E. Henney was the acting Commissioner at the time this case was filed.

States of America. Plaintiffs challenge the FDA's denial of a health claim application for saw palmetto.

This matter is before the Court on Plaintiffs' Motion for Summary Judgment and Defendants' Motion to Dismiss. Plaintiffs claim the FDA's decision violates the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.* (1972) , the Administrative Procedure Act ("APA"), 5 U.S.C. § 706 *et seq.* (1996), the First Amendment, canons of statutory interpretation, and the Supremacy Clause. Defendants move to dismiss for failure to state a claim upon which relief can be granted, Fed. R. Civ. P. 12 (b)(6), arguing that the FDA properly denied Plaintiffs' health claim application based on its classification of the saw palmetto claim as a drug claim. Upon consideration of Plaintiffs' and Defendants' Motions, Oppositions, Replies, the October 28, 2002, Motions Hearing, and the entire record herein, for the reasons discussed below, Defendants' Motion to Dismiss is granted, and Plaintiffs' Motion for Summary Judgment is denied.

I. Background

A. Statutory and Regulatory Framework

Prior to November 8, 1990, the FDCA provided that dietary supplements—including the saw palmetto supplements at issue in this case—would be regulated as a food, unless their intended use was as a drug.[3] In other words, if a dietary supplement's label contained a disease-specific claim,[4] that supplement was subject to the FDA's drug approval and drug labeling requirements. *See* H.R. Rep. No.

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[3] "Food" is defined, in part, as "articles used for food or drink." 21 U.S.C. § 321(f)(1). "Drugs" are defined, in part, as "articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease." 21 U.S.C. § 321(g)(1)(B).

[4] A "label" is defined as "a display of written, printed, or graphic matter upon the immediate container of any article." 21 U.S.C. § 321(k).

101-538, at 9 (1990) ("House Rep."); 21 U.S.C. §§ 321(g) (1) (B) and 355 (1996).

However, during the mid-1980s companies began making disease-specific claims about foods with increasing frequency and without the approval of the FDA. *See* House Rep. at 9. In response, Congress amended the FDCA through enactment of the Nutrition Labeling and Education Act ("NLEA") on November 2, 1990. Pub. L. No. 101-535, 104 Stat. 2353 (1990). Passage of the NLEA was intended to address concerns that the FDA had brought "virtually no enforcement actions" against the types of claims it had previously prohibited by clarifying and strengthening "the [FDA's] legal authority . . . to establish the circumstances under which claims may be made about the nutrients in foods." House Rep. at 7, 9.

The NLEA liberalized the FDCA to permit health claims to be "made in the label or labeling of [a] food which expressly or by implication . . . characterizes the relationship of any nutrient . . . to a disease or a health-related condition." 21 U.S.C. § 343(r)(l)(B). However, Congress clearly stated that the NLEA and FDA regulatory standards were to concern "only nutrients or substances in foods that 'nourish' and . . . [not] other, non-nutritive substances in foods." House Rep. at 7. Congress delegated to the FDA the task of developing a procedure and standard for approving health claims for dietary supplements, providing that health claims

> made with respect to a dietary supplement of vitamins, minerals, herbs, or other similar nutritional substances . . . shall be subject to a procedure and standard, respecting the validity of such a claim, established by regulation of the Secretary.

21 U.S.C. § 343(r)(5)(D). Thus, under the NLEA, a dietary supplement health claim is not automatically subject to the FDCA's far more extensive and demanding approval and labeling requirements for drugs so long as the claim is made

in accordance with other sections of the statute, including 21 U.S.C. § 5 343(r)(5)(D).

In 1993, the FDA responded to the NLEA by promulgating 21 C.F.R. §§ 101.14 and 101.70, which explained the standards and procedures for FDA consideration of nutrient-disease claims. The FDA chose the same standard for authorizing dietary supplement health claims as the NLEA prescribed for authorizing food health claims—significant scientific agreement. *See* 21 C.F.R. §§ 101.14.[5] In requesting authorization for a health claim, a party first submits a petition with the proposed health claim, accompanied by supporting evidence. *See id.* §§ 101.70 (a)-(i). The FDA must then notify the applicant within 100 days whether the request will be denied or else "filed" for further review. *See* § 101.70(j) (2). If further review is warranted, within the next 90 days the FDA must either deny the petition or publish a proposed regulation authorizing the health claim. *See id.* § 101.70(j)(3). If the FDA publishes a proposed rule authorizing a health claim, the FDA must publish a final regulation approving or denying the claim within 270 days of the date of publication. *See id.* § 101.70(j)(4).

In 1994, Congress passed the Dietary Supplement Health and Education Act of 1994 ("DSHEA"), Pub. L. No. 103-417, 108 Stat. 4325 (1994), to further recognize "the importance of

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[5] In 1999, the Court of Appeals for the District of Columbia ordered the FDA to further define the "significant scientific agreement" standard for evaluating dietary supplement health claims. *Pearson v. Shalala*, 164 F.3d 650, 655 (D.C. Cir. 1999). In response, the FDA issued "Guidance for the Industry: Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements." Available at http://www.cfsan.fda.gov/~dms/ssaguide.html ("Guidance Report"). The Guidance Report stated that significant scientific agreement meant that "the validity of the relationship is not likely to be reversed by new and evolving science, although the exact nature of the relationship may need to be refined." *Id.* at 2.

nutrition and the benefits of dietary supplements to health promotion and disease prevention." *Id.* at § 2(2). The DSHEA clarified the FDA's role in authorizing health claims by creating "a rational Federal framework . . . to supersede the current ad hoc, patchwork regulatory policy on dietary supplements" to protect consumers' right of access to "safe dietary supplements. . . to promote wellness." *Id.* at § 2(15). Passage of the DSHEA attempted to further clarify the authorization of dietary supplement health claims by including within the FDCA a dietary supplement definition and an amended drug definition.[6]

B. Procedural History

On May 25, 1999, Plaintiffs filed a health claim petition with the FDA seeking approval for the labels of saw palmetto supplements[7] to include the following health claim:

> Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce

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[6] The FDCA definitions of "drug", and "dietary supplement," as amended by the NLEA and the DSHEA, are set forth in § 321 as follows:

> (g) (1) The term "drug" means. . . .(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals. . . .A food or dietary supplement for which a claim, subject to . . . sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim.
>
> (ff)The term "dietary supplement"—
>
> > (1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:. . . (C) an herb or other botanical . . . .
> >
> > Except for purposes of [the drug definition at § 321(g)], a dietary supplement shall be deemed to be a food within the meaning of this Act.

[7] Specifically, the saw palmetto in Plaintiffs' dietary supplements is the *n*-hexane lipidosterolic extract of the pulp and seed (fruit) of the dwarf American palm, *Seronoa repens*. A.R. at 10.

> voiding urgency associated with mild benign prostatic hyperplasia (BHP).

Administrative Record ("A.R.") at 21-22. In accordance with FDA regulations, Plaintiffs included scientific evidence supporting their claim. *See* A.R. at 121-397. Plaintiffs also requested that the FDA "approve the claim with such disclaimer or disclaimers as the agency reasonably deemed necessary to avoid any potentially misleading connotation." A.R. at 10; *see Pearson v. Shalala*, 164 F.3d 650 (D.C. Cir. 1999) (Because the First Amendment favors speech disclosure over speech suppression, the FDA may not completely ban potentially misleading health claims but should allow such claims with an appropriate disclaimer.).

On June 7, 1999, the FDA acknowledged receipt of the Plaintiffs' health claim petition, and on September 1, 1999, the FDA accepted the petition for filing. *See* A.R. at 398, 406. The Plaintiffs' petition was denied under operation of law on December 1, 1999, because the FDA allowed 90 days to pass without issuing a decision. *See* A.R. at 1175. The FDA stated that the denial was necessary because the prescribed time frame was insufficient to resolve the "important and novel issue . . . whether health claims for foods (including dietary supplements) may encompass [a claim of an effect on an existing disease] or whether such a claim is appropriate only on a product that has been shown to meet the safety and efficacy requirements for drugs." *Id.*

On December 7, 1999, the Plaintiffs filed this suit seeking declaratory and injunctive relief in light of the FDA's denial of their health claim petition. The action was stayed pending FDA reconsideration of its decision, and on April 4, 2000, the FDA held public hearings to determine whether the Plaintiffs' saw palmetto claim was a health claim or a drug claim under the FDCA. Upon consideration of the hearings and other comments, the FDA issued a formal letter on May 26, 2000,

providing further explanation of its refusal to process the Plaintiffs' saw palmetto petition. *See* A.R at 721.

The FDA concluded that "claims about effects on existing diseases do not fall within the scope of the health claims provisions in 21 U.S.C. § 343(r) and therefore may not be the subject of an authorized health claim." A.R. at 723. With regard to Plaintiffs' proposed health claim, the FDA found that

> [The] petition clearly identifies the intended use of saw palmetto extract products bearing that proposed claim as the treatment of the urinary symptoms of BPH. The proposed model claim . . . explicitly describes the mitigation of disease by treating its symptoms and establishes the intended use of products bearing the claim as drugs.

A.R. at 728. The FDA stated that its decision was based on the language and legislative history of the FDCA, prior agency interpretations of claims to treat disease, and concern that men would miss early diagnosis of prostate cancer by self-medicating with saw palmetto.

II. Standard of Review

A complaint should not be dismissed for failure to state a claim "unless it appears beyond doubt that the plaintiff can prove no set of facts in support of his claim which would entitle him to relief." *Conley v. Gibson*, 355 U.S. 41, 45-46 (1957); *Davis v. Monroe County Bd. of Educ.*, 526 U.S. 629, 654 (1999). To that end, the complaint is construed liberally in the plaintiffs' favor, and the court grants plaintiffs the benefit of all inferences that can be derived from the facts alleged. *Shear v. National Rifle Ass'n of Am.*, 606 F.2d 1251, 1253 (D.C. Cir. 1979). However, the court need not accept inferences drawn by plaintiffs if such inferences are unsupported by the facts set out in the complaint, nor must the court accept legal conclusions cast in the form of factual

allegations. *Kowal v. MCI Communications Corp.*, 16 F.3d 1271, 1276 (D.C. Cir. 1994) (internal citations omitted).

III. Analysis

Plaintiffs argue that the central issue in this case is whether the FDA may deny their petition and indefinitely suppress the saw palmetto health claim. Plaintiffs contend that the FDA's refusal to evaluate the claim under 21 U.S.C. § 343(r)(5)(D) violates both the FDCA and the APA and constitutes a blanket ban on commercial speech in violation of the First Amendment. Plaintiffs argue that a claim made in accordance with § 343(r)(5)(D) is a health claim for a dietary supplement and cannot be regulated by the FDA as a drug claim because Congress clearly intended health claims to include *any* nutrient-disease claim, not just risk reduction claims.

However, Defendants argue that when reading the health claims provision in the context of the entire FDCA, Congress never intended to limit the statute's central purpose of drug regulation. Thus, Defendants contend that the statute only allows health claims regarding disease prevention and mandates denial of any claims falling outside that scope—i.e, claims containing a non-preventative intent included in the FDCA's drug definition, such as providing treatment for an existing disease. Defendants argue that the FDA's statutory construction violates neither the FDCA nor the APA because the FDCA's definitions for dietary supplements and drugs are not mutually exclusive. Furthermore, Defendants argue that the FDA's decision to ban Plaintiffs' saw palmetto claim, given its classification as a drug claim, is in accordance with First Amendment principles for government regulation of commercial speech.

A. The FDA's Determination That It May Authorize Only Those Health Claims Regarding Disease Prevention Violates Neither the FDCA Nor the APA.

Plaintiffs contend that the FDA's classification of the saw palmetto claim as a drug claim violates both the FDCA and the APA because the health claims provision in § 343(r)(1)(B) precludes dietary supplement claims from being categorized as drug claims under § 321(g)(1). This argument presents an issue of statutory interpretation governed by the well-known analytic framework set forth in *Chevron USA Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 843-45 (1984). *Accord Young v. Community Nutrition Institute*, 476 U.S. 974, 980-811 (1986) (applying Chevron analysis to the FDA's interpretation of the FDCA).

Under step one of the *Chevron* analysis, the court asks "whether Congress has directly spoken to the precise question at issue." *Id.* 467 U.S. at 842. If the intent of Congress is clear, "that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Id.* 467 U.S. at 842-43. However, if the statute is "silent or ambiguous with respect to the specific issue," the court proceeds to step two of the Chevron analysis and asks "whether the agency's answer is based on a permissible construction of the statute." *Id.*, 467 U.S. at 843. Thus, to hold the FDA's present interpretation of the FDCA erroneous, the court must "conclude that [the FDA's] interpretation either ran athwart a clear mandate of Congress, or was an unreasonable one." *Troy Corporation v. Browner*, 120 F.3d 277, 283 (D.C. Cir. 1997).

1. *Chevron* Step One

Turning to the first stage of the *Chevron* analysis, the Court must determine whether Congress expressed clear intent regarding the proper scope of health claims allowed under the

FDCA. In determining congressional intent, a court must employ "traditional tools of statutory construction," including "the statute's text, legislative history, and structure, as well as its purpose." *Bell Atlantic Telephone Companies v. F.C.C.*, 131 F.3d 1044, 1047 (D.C. Cir. 1997).

The language of § 343(r)(1)(B) provides that a health claim for a dietary supplement is a claim that "characterizes the relationship of any nutrient . . . to a disease or health-related condition." 21 U.S.C. § 343(r)(1)(B). Plaintiffs contend that by enacting § 343(r)(1)(B), Congress clearly intended health claims for dietary supplements to include any nutrient-disease claim and did not intend to limit these claims to disease risk reduction claims. However, Defendants argue that, when read in the context of the whole FDCA, it is clear that Congress never intended § 343(r)(1)(B) to limit the statute's core function of drug regulation. *See F.D.A. v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 132-133 (2000) (When determining whether Congress has specifically addressed the question at issue, "the words of a statute must be read . . . with a view to their place in the overall statutory scheme.") (internal citations and quotations omitted). Defendants thus argue that Congress intended the FDA to evaluate the validity of a health claim under both the dietary supplement and drug provisions of the FDCA.

Accordingly, the Court must examine not only the language of § 343(r)(1)(B) but also the provision regarding FDA health claim approval and other relevant definitions. Approval of a dietary supplement health claim "shall be subject to a procedure and standard, respecting the validity of such claim, established by regulation of the Secretary [of the FDA]." 21 U.S.C. § 343(r)(5)(D). A dietary supplement is a product "intended to supplement the diet that bears or contains . . . an herb or other botanical" that will be deemed a food "[e]xcept for purposes of [the drug definition at § 321(g)]." 21 U.S.C. § 321(ff)(1)(c). A drug is a product

"intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1)(B). While § 343(r)(5)(D) clearly indicates that the FDA has authority to determine the standards regarding health claims for dietary supplements, it is unclear how those standards affect the approval of health claims for products that treat an existing disease.

Plaintiffs argue that if the dietary supplement definition is not read to supersede the drug definition, all health claims could be regulated as drugs given their intended use for "prevention of disease." However, Congress rejected Plaintiffs' view when it refused to add a provision to the DSHEA's drug definition stating that, subject to certain exceptions, "[t]he term 'drug' does not include a dietary supplement as defined in paragraph (ff). . . ." 140 Cong.Rec. S11706 (daily ed. Aug. 13, 1994). *See also U.S. v. Ten Cartons, More or Less, of an Article Ener-B Vitamin B-12*, 72 F.3d 285, 287 (2d Cir. 1995) (A product deemed a dietary supplement under § 321(ff) could also be classified as a drug under § 321(g)(1) because Congress considered and rejected the provision to exclude dietary supplements from drug classifications). Thus, Plaintiffs' argument has little force. *See INS v. Cardoza-Fonseca*, 480 U.S. 421, 442-43 (1987) ("Few principles of statutory construction are more compelling than the proposition that Congress does not intend sub silentio to enact statutory language that it has earlier discarded in favor of other language.") (internal citations and quotations omitted).

Plaintiffs also contend that congressional intent to restrict health claims from classification as drug claims is found in other language added to the drug definition by the DSHEA, stating that

> A food or dietary supplement for which a claim, subject to . . .sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section

> 343(r) of this title is not a drug solely because the label or the labeling contains such a claim.

21 U.S.C. § 321(g)(1). However, Defendants argue that the term "solely" indicates that Congress still intended the FDA to retain its long-established discretion to classify a claim as a drug claim if it provided adequate grounds for the classification.

In this case, the FDA has provided a further explanation for its decision to classify Plaintiffs' claim as a drug claim—i.e., the proposed claim goes beyond risk reduction and purports to treat a disease. The FDA argues that because the FDCA's definitions for dietary supplements and drugs are not mutually exclusive, it is authorized to determine that health claims for dietary supplements are actually drug claims when the claim is directed at disease treatment. *See Bell Atlantic Telephone Co.*, 131 F. 3d at 1048 (When attempting to understand "the relationship between two different provisions within the same statute, [a court] must analyze the language of each to make sense of the whole [statute]."). Congress' intent regarding the scope of health claims is not clear on the face of the FDCA, as amended by the NLEA and the DSHEA, given the interconnectedness of the statute's provisions.

Unfortunately, the legislative histories of the FDCA, NLEA, and DSHEA do not demonstrate a clear congressional intent with regard to the appropriate scope of health claims. There is no question that the legislative intent behind enactment of the original FDCA was to protect the public from unsafe drugs. *See U.S. v. Undetermined Quantities of . . . Vetrinary Drug*, 22 F.3d 235, 238 (10th Cir. 1994) (citing *U.S. v. Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 789 (1969)) (Provisions of the FDCA are to be liberally construed consistent with the Act's overriding purpose of protecting public health).

In amending the FDCA through the NLEA, Congress created a framework for authorization of health claims but also delegated full authority to the FDA to adopt whichever standard the agency deemed most appropriate for approving such claims. *See* 136 Cong. Rec. H12953 (Oct. 26, 1990) (The House Floor Manager stated that "the FDA is given the discretion to define both the procedure and the standard [for approving health claims] because the principals in the Senate could not agree."). While the NLEA provided the statutory authority for authorizing health claims, it clearly gave the FDA wide discretion in approving such claims. *See* House Rep. at 8 (Health claims "may not be made unless [they are] consistent with a final regulation issued by the FDA.").

Nor do the DSHEA amendments demonstrate any clear congressional intent with respect to the specific scope of health claims. Here too, the legislative history is ambiguous. It is clear that Congress intended the FDA to establish a more principled regulatory framework for authorizing health claims in order to provide consumers with more access to such information. Pub.L. No. 103-417, 108 Stat. 4325 at § 2 (15). However, Congress specifically stated that the amendments were added to recognize "the benefits of dietary supplements to health promotion and disease *prevention*." *Id.* at § 2 (2) (emphasis added).

Furthermore, Congress issued a Statement of Agreement for the DSHEA that compromised the amendments' "entire legislative history." 140 Cong. Rec. S14801 (Oct. 7, 1994). The sponsors of the bill intended "that no other reports or statements be considered as legislative history for the bill." *Id.* Because the Statement of Agreement provides explanations for only four DSHEA amendments and does not include any statement regarding the appropriate scope of health claims, the Court finds that the Statement of Agreement further demonstrates an overall lack of specific intent regarding the meaning of the DSHEA amendments in

the context of the whole FDCA. *See also Pharmanex v. Shalala*, 221 F.3d 1151, 1158 (10th Cir. 2000) (The court found that the meaning of DSHEA provisions were "not elucidated, but rather [became] less clear" by the Statement of Agreement.).

In this case, the Court finds an absence of a clear congressional intent with respect to the appropriate scope of health claims. Given the ambiguity inherent in the FDCA' s intertwined definitions for drugs and dietary supplements, the lack of decisive legislative history, and the FDCA's dual function of regulating both drugs and dietary supplements, the Court determines that "Congress has [not] directly spoken to the precise question at issue." *Chevron*, 467 U.S. at 842.

2. *Chevron* Step Two

Because the Court has determined that the intent of Congress with respect to the scope of health claims is ambiguous, analysis of the FDA's decision under the second stage of *Chevron* is required. In the second stage, a court must evaluate the same text, history, and purpose used in the first stage, but instead of determining "whether these convey a plain meaning that *requires* a certain interpretation," the court will determine ''whether these *permit* the interpretation chosen by the agency." *Bell Atlantic Telephone Co.*, 131 F.3d at 1049 (emphasis in original). At stage two, a court "need not conclude that the agency construction was the only one it permissibly could have adopted to uphold the construction, or even the reading the court would have reached if the question originally had arisen in a judicial proceeding." *Chevron*, 467 U.S. at 843 n.11. The court need merely find that the agency's choice is a rational one. *See Young*, 476 U.S. at 981 (The FDA's interpretation of an ambiguous FDCA provision was sufficiently rational "to preclude a court from substituting its judgment for that of the FDA.").

Courts have long upheld FDA decisions to classify products as drugs based on their intended use. *See Action on*

Smoking and Health v. Harris, 655 F.2d 235 (D.C. Cir. 1980) (The FDA's refusal to classify cigarettes as a drug was not arbitrary and capricious because Plaintiffs had failed to prove that the manufacturers had expressed an intent covered by the FDCA's drug definition.); *National Nutritional Foods Assoc. v. Mathews*, 557 F.2d 325, 333 (2d Cir. 1977) (The "vendor's intent in selling the product to the public is the key element" in the FDCA drug definition.).

Furthermore, courts have found that because the FDCA definitions of dietary supplements and drugs are not mutually exclusive, FDA regulation may properly focus on intent. *See Ten Cartons . . . Ener-B Vitamin B-12*, 72 F.3d at 287 (The FDA may regulate an article as a drug pursuant to § 321(g)(1)(C) whether or not it is a "dietary supplement" within the meaning of § 321 (ff).); *U.S. v. Writers & Research, Inc.*, 113 F.3d 8 (2d Cir. 1997) (A homeopathic substance is subject to FDCA requirements for drugs if it is promoted as a treatment or cure for an existing disease.).

Plaintiffs argue that the FDA has already interpreted the FDCA to allow health claims for disease treatment. For example, one of five model health claims suggested by the FDA for the dietary fat and cholesterol-coronary heart disease relationship states that a "healthful diet low in saturated fat, total fat, and cholesterol . . . may lower blood cholesterol levels and may reduce the risk of heart disease." 21 C.F.R 101.75(e)(3) (2002). Plaintiffs contend that this health claim goes beyond risk prevention because it includes a claim to lower blood cholesterol, which is treating an existing disease. *See also* 21 C.F.R 101.77(e)(2) (2002) (A model dietary fiber-coronary heart disease health claim also states that eating a diet high in dietary fiber "may lower blood cholesterol levels and reduce your risk of heart disease."). However, Defendants argue that these claims are primarily concerned with risk reduction of heart disease, not the

treatment of an existing disease. In fact, the FDA's rulemaking clearly stated that these claims linked "dietary factors to heart disease *risk* via the *intermediate* mechanism of reducing blood LDL-cholesterol levels . . . ." 58 Fed. Reg. 2552, 2573 (1993) (emphasis added).

Moreover, reports relied upon by Congress in enacting the NLEA clearly focused on the role of diet in reducing disease risk, *not* in treating an existing disease. *See* House Rep. at 9 (referring to the Surgeon General's "Report on Nutrition and Health" (1988) for the argument that certain diets "can reduce the *risk* of chronic disease") and 13-14 (relying upon the National Research Council's "Diet and Health Implications for Reducing Chronic Disease *Risk*" (1989)) (emphasis added).

In this case, the FDA concluded that Plaintiffs' health claim indicated that saw palmetto's intended use was purely pharmacological. The proposed claim addresses only BHP symptom treatment and does not include any claim of disease prevention, bolstering FDA concerns that approval of the claim would not provide an adequate level of protection to vulnerable consumers. In fact, the FDA previously withdrew over-the-counter approval for saw palmetto by concluding that while "saw palmetto 'probably' provides some 'minimal' [BHP] symptomatic relief" it was concerned that "as long as only the symptoms of the disease [were] relieved, men with BHP may be lulled into a false sense of security" and postpone medical examinations necessary for treatment of BHP, diagnosis of secondary complications, and screening for prostate cancer. A.R. at 729 (*citing* to 55 Fed. Reg. 6926 (1990)).

The FDCA, as amended by the NLEA and the DSHEA, establishes both the FDA's authority to regulate drugs and dietary supplements and the FDA's responsibility to protect consumers. The FDA has decided that approval of a health claim with a purely pharmacological purpose would not

provide an adequate level of consumer protection. As the language, structure, and legislative history of the FDCA do not clearly state the appropriate scope of health claims for dietary supplements, the Court finds the FDA's decision to limit approved health claims to those involving disease risk reduction is both permissible and reasonable under the second stage of the *Chevron* analysis.

3. The APA

Under the APA, an agency's action may be set aside only if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2) (A). In making this finding, the court "must consider whether the decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 416 (1971). The court's role is to ensure that the agency's decision was based on relevant factors and not a "clear error of judgment," not substitute its judgment for that of the agency. *Id.*, 401 U.S. at 416. If the "agency's reasons and policy choices . . . conform to certain minimal standards of rationality . . . the rule is reasonable and must be upheld." *Small Refiner Lead Phase-Down Task Force v. EPA*, 705 F.2d 506, 521 (D.C. Cir 1983) (citation omitted). This standard presumes the validity of agency action. *Ethyl Corp. v. EPA*, 541 F.2d 1, 34 (D.C. Cir. 1976) (en banc), *cert. denied*, 426 U.S. 941 (1976).

As explained above, the FDA has provided an adequate rationale for its determination that the FDCA, as amended by the NLEA and the DSHEA, authorizes the FDA to deny health claims aimed primarily at treatment for an existing disease. Therefore, the FDA's decision to deny the saw palmetto claim as a drug claim, given its intended treatment of BHP, was neither arbitrary nor capricious. In addition, since the FDA's interpretation of the FDCA was permissible under the two-step analysis of *Chevron*, its

decision was not contrary to law. Accordingly, the FDA did not violate the APA in denying Plaintiffs' saw palmetto health claim petition.

B. The FDA's Decision to Deny Plaintiffs' Health Claim Does Not Violate the First Amendment.

Plaintiffs argue that the saw palmetto claim is either scientific or commercial speech protected by the First Amendment. However, it is "undisputed that [ ] restrictions on [ ] health claims are evaluated under the commercial speech doctrine." *Pearson*, 164 F.3d at 655 (*citinq Bolger v. Youngs Drug Prods. Corp.*, 463 U.S. 60, 67-68 (1983)). Therefore, the FDA's refusal to authorize Plaintiffs' proposed claim must be evaluated under the analytical framework established in *Central Hudson Gas & Elec. Corp. v. Public Serv. Comm'n of New York*, 447 U.S. 557 (1980). *See also Thompson v. Western States Med. Ctr.*, __ U.S. __, 122 S.Ct. 1497 (2002) (applying the *Central Hudson* analysis to FDA regulations concerning advertising and promotion of compounded drugs).

Under *Central Hudson*, the reviewing court must conduct a four-part analysis for evaluating legislative restrictions on commercial speech. First, the court must determine whether the expression is protected by the First Amendment—i.e., whether "the speech concerns lawful activity and is not misleading." *Western States*, 122 S.Ct at 1504. A complete ban on commercial speech is only appropriate where the government proves that "the expression itself was flawed in some way, either because it was deceptive or related to unlawful activity." *Central Hudson*, 477 U.S. at 566 n.9. If the speech is protected, the court must determine "whether the asserted government interest is substantial." *Central Hudson*, 447 U.S. at 566. If the government interest is substantial, the court must determine "whether the regulation directly advances the governmental interest asserted." *Central Hudson*, 447 U.S. at 566. Finally, the court must deter-

mine "whether [the regulation] is not more extensive than is necessary to serve that interest." *Central Hudson*, 447 U.S. at 566.

Plaintiffs argue that the FDA's denial of the saw palmetto health claim cannot meet the *Central Hudson* test as articulated by *Pearson*, because it impermissibly restricts commercial speech by not allowing "the Plaintiffs' health claims to be made with such disclaimers as are reasonably necessary to avoid a misleading connotation." Pls.' Mot. for Summary J. at 42. While the *Pearson* decision did restrict FDA regulation of potentially misleading speech in health claims, Plaintiffs mistakenly construe the FDA's current decision to deny the saw palmetto health claim petition as a decision based on misleadingness. In this case, the Court has determined that the FDA has reasonably interpreted the FDCA to conclude that "claims about the effects on existing disease do not fall within the scope of the health claim provisions in 21 U.S.C. § 343(r) and therefore may not be the subject of an authorized health claim." A.R. at 723. Because the FDA determined that the saw palmetto claim was a drug claim for disease treatment, it concluded that the claim was an *unlawful* health claim and thus denied Plaintiffs' petition.

As there is no doubt that unlawful speech can be banned under the first step of the *Central Hudson* analysis, the FDA's prohibition of Plaintiffs' saw palmetto claim does not violate the First Amendment. *See id.* , 447 U.S. at 563-64 ("[T]here can be no constitutional objection to the suppression of commercial messages that do not accurately inform the public about lawful activity. The government may ban . . . commercial speech related to illegal activity."); *44 Lisuormart, Inc. v. Rhode Island*, 517 U.S. 484, 497 n.7 (1996) ("[T]he First Amendment does not protect commercial speech about unlawful activities.").

IV. Conclusion

The FDA's denial of Plaintiffs' saw palmetto claim did not violate the FDCA, APA, or First Amendment. The FDA's interpretation of the various provisions of the FDCA to permit only disease prevention health claims was reasonable given the ambiguity of the statute; therefore, its decision to deny Plaintiffs' claim based on this interpretation is neither arbitrary nor capricious nor contrary to law. For the reasons discussed above, Plaintiffs' Motion for Summary Judgment is denied and Defendants' Motion to Dismiss is granted. An Order will issue with this Opinion.

Date: Jan. 3, 2003

/s/ GLADYS KESSLER
GLADYS KESSLER
United States District Judge

Copies to:

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

Civil Action
NO. 99-3247 (GK)

[FILED JAN 03 2003]

JULIAN M. WHITAKER, M.D., et al.,
Plaintiffs,

v.

TOMMY G. THOMPSON, Secretary,
Department of Health and Human Services, *et al.*,
Defendants,

ORDER

This matter is before the Court on Plaintiffs' Motion for Summary Judgment [#19] and Defendants' Motion to Dismiss [#20]. Upon consideration of Defendants' and Plaintiffs' Motions, Oppositions, Replies, the October 28, 2002, Motions Hearing, and the entire record herein, for the reasons stated in the accompanying Memorandum Opinion, it is this day of January, 2003, hereby

ORDERED, that Defendants' Motion to Dismiss [#20] is granted; and it is further

ORDERED, that Plaintiffs' Motion for Summary Judgment [#19] is denied.

/s/ Gladys Kessler
GLADYS KESSLER
United States District Judge

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APPENDIX C

DEPARTMENT OF HEALTH AND HUMAN SERVICES

[SEAL]

Public Health Service
Food and Drug Administration
Washington, DC
May 26, 2000

JONATHAN W. EMORD
EMORD & ASSOCIATES, P.C.
1050 Seventeenth Street, N.W.
Suite 600
Washington, D.C. 20036

Dear Mr. Emord:

This letter concerns your health claim petition (Docket Number 99P-3030) submitted to the Food and Drug Administration (FDA) on May 25, 1999, on behalf of Julian Whitaker, M.D., Durk Pearson and Sandy Shaw, American Preventive Medical Association, and Pure Encapsulations, Inc. The petition requests that FDA authorize a health claim concerning the relationship between dietary supplements containing saw palmetto (specifically, the *n*-hexane lipidosterolic extract of the pulp and seed (fruit) of the dwarf American palm, *Serenoa repens*) and benign prostatic hyperplasia (BPH). The model claim set forth in the petition is: "Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH)."

I. Background

In accordance with the procedures in 21 C.F.R. § 101.70 (j)(2), the agency filed your petition for comprehensive review on September 1, 1999. The petition was denied by

operation of law on December 1, 1999, under section 403(r)(4)(A)(i) of the Federal Food, Drug and Cosmetic Act (FFDCA) (21 U.S.C. § 343(r)(4)(A)(i)) and 21 C.F.R. § 101.70(j)(3)(iii), which provide that if FDA does not propose a regulation to take the action proposed in a health claim petition within 90 days after the agency has filed the petition, the petition is deemed to be denied. On December 1, we forwarded a letter to you explaining that we were not proposing a rule because we were unable to resolve, within the statutorily prescribed timeframe, the threshold issue presented by the petition: whether a claim about an effect on an existing disease is within the scope of the food[1] labeling health claims provisions of the FFDCA.

All of the health claims that FDA has authorized since the passage of the Nutrition Labeling and Education Act of 1990 (NLEA) have been claims about reducing the risk of contracting a particular chronic disease. In contrast, the saw palmetto extract claim for which you have requested authorization represents a claim about an effect on an existing disease - namely, a claim to relieve symptoms of BPH. The claim would therefore be directed at men who have already contracted BPH. To date, authorized health claims have been targeted to the general population or to a population subgroup whose members are at risk for a particular disease, but not to those who already have the disease.

FDA held a public meeting on April 4, 2000, to solicit public comment on, among other issues, whether claims about effects on an existing disease may qualify as health claims. The agency also created a docket (Docket No. 00N-0598) to receive written comments. The docket was open for

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[1] When the term "food" is used in this letter, it encompasses both conventional foods and dietary supplements. Except for purposes of the drug definition in 21 U.S.C. § 321(g)(1), dietary supplements are deemed to be foods under the FFDCA. 21 U.S.C. § 321(ff).

more than 30 days, from March 16, 2000, through April 19, 2000. Eighty-nine written comments and prepared statements were received and filed in the docket; thirty-four of these comments expressed an opinion on whether claims about effects on an existing disease may qualify as health claims.[2] Fourteen people spoke on this issue at the meeting, including five panelists specifically invited to discuss it.

Written comments in the docket and oral comments at the meeting show basically two opposing opinions on this issue. One group of comments pointed to the broad language of 21 U.S.C. § 343(r)(1)(B), which defines a health claim as a claim that "characterizes the relationship of any nutrient . . . to a disease or health-related condition." These comments argued that this language shows that Congress intended to permit any truthful claim about disease as a health claim on foods. The other main view expressed in the comments was that Congress enacted the NLEA health claim provisions in response to manufacturers' desire to use information about diet and long-term health to promote food products and that Congress did not intend to undermine the established premarket drug approval procedures for products bearing claims about mitigation or treatment of disease. Some of the comments adopting the latter view raised public health concerns about allowing foods to make health claims for effects on existing diseases, both generally and in the context of saw palmetto dietary supplements and BPH.

II. Scope of Issue and Explanation of Terminology

This letter states FDA's position on whether certain types of disease claims for foods fall within the scope of the health claim provisions in 21 U.S.C. § 343(r).

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[2] The relevant comments and prepared statements from the public meeting docket and the transcript of the public meeting have been included in the docket of this proceeding.

Your proposed claim for saw palmetto extract is a claim to relieve the symptoms of an existing disease. Such a claim could be characterized as a claim to treat disease, a claim to mitigate disease, or both. In the absence of health claim authorization, both types of claims subject a food to regulation as a drug under 21 U.S.C. § 321(g)(1)(B), which encompasses articles "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease." FDA believes that claims to treat, mitigate, and cure disease are closely related, in that all are claims to have an effect on an existing disease. Because of this close relationship and because the statute and legislative history support treating them the same way for purposes of the issue your petition presents, this letter states FDA's position on that issue with respect to all three types of claims. Although FDA has not defined the exact meaning of these three terms or the extent to which they may overlap, the agency believes that there is no meaningful distinction between them with respect to the scope of the health claims provisions in 21 U.S.C. § 343(r). For simplicity, the term "treat" will be used as a synonym for "treat, mitigate, or cure" throughout the remainder of the letter.

III. Agency Decision

After thoroughly reviewing the relevant statutory provisions and legislative history, FDA's past statements on this issue, and the comments we have received on it, we have concluded that claims about effects on existing diseases do not fall within the scope of the health claim provisions in 21 U.S.C. § 343(r) and therefore may not be the subject of an authorized health claim. We have come to this conclusion after carefully considering the language and structure of the NLEA and the FFDCA as well as the public health importance of ensuring that claims to treat disease be substantiated by the appropriate level of evidentiary support to

provide protection for patients who are already sick and, therefore, especially vulnerable.

A. Pre-NLEA FDA Proposals and the Enactment of the Medical Foods Definition

Drugs have always been permitted to claim an effect on disease. The term "drug" is defined, in part, as an article "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1)(B). Thus, foods that claim an effect on disease generally have been subject to regulation as drugs.

FDA first proposed to allow a limited *subset* of such claims in food labeling in 1987. FDA based its original 1987 proposal on health claims for foods, and subsequent reproposal in 1990, on the increasingly prevalent scientific view that good nutrition and diet are essential components of health protection and promotion efforts. *See* 52 Fed. Reg. 28843 (1987); 55 Fed. Reg. 5176 (1990). This view, and the related view that making information about diet and health available to consumers in food labeling would assist such efforts, had been embraced by a broad spectrum of society, including industry, consumer advocacy groups, and professional societies. *See* 52 Fed. Reg. at 28844. Both proposed rules, as well as the scientific publications cited to support them, focused on diet as a means of reducing the risk,[3] or forestalling the premature onset, of chronic diseases, such as cancer and coronary heart disease. The preamble to the 1987 proposed rule stated that health claims "should not imply that a particular food be used as part of a drug-like treatment or therapy oriented approach to health care." 52 Fed. Reg. at 28845. The regulatory text of the 1990 proposed rule would have explicitly limited acceptable health claims to claims about "the value that ingestion (or reduced ingestion) of a

[3] Throughout this letter, the phrase "reducing the risk" of a disease refers to reducing the risk of contracting the disease.

dietary component may have in either lowering the risk, or forestalling the premature onset, of a particular chronic disease condition." 55 Fed. Reg. at 5192.

Several citizen petitions requesting that FDA permit health claims similarly limited the scope of health claims for foods. A petition from a dietary supplement trade association (Docket No. 85N-0061/CP3) included recommended criteria that specifically excluded "therapeutic" statements. The criteria were designed to differentiate "therapeutic" statements from "nutritional" statements. Another petition from a conventional food trade association (Docket No. 85N-0061/CP1) requested FDA to permit claims about "the relationship between the presence or absence of a particular dietary property provided by [a] food as part of a well-balanced diet and the *maintenance of health or wellness*, including the *incidence* of specific diseases, symptoms, or disorders" (emphasis added). A petition from a consumer group (Docket No. 85N-0061/CP5) would have limited health claims to claims about reducing the risk of a disease.

Hence, before the passage of NLEA, health claims were envisioned as being intended to assist the general population in maintaining good health (or avoiding poor health), and not to treat existing disease.

In 1988, Congress enacted legislation that, among other things, provided for another type of disease-related claim for a limited subset of foods. The Orphan Drug Amendments established a new statutory product category called "medical foods." A "medical food" is defined as "a food which is formulated to be consumed or administered enterally (i.e., via the digestive system) under the supervision of a physician and which is intended for the specific *dietary management* of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation." 21 U.S.C. 360ee(b)(3)

(emphasis added).[4] Thus, medical foods are foods that are intended to affect an existing disease through a nutritional mechanism.

B. The Statute and the Legislative History

In the NLEA, Congress authorized foods to carry health claims without becoming drugs, prescribing conditions under which a food may bear a health claim without being misbranded and creating a partial exemption from the drug definition for foods that meet those conditions. The health claim provisions of the NLEA are similar in many ways to the 1990 FDA health claims proposal, although the NLEA establishes more elaborate procedural requirements for health claims. Both emphasize dietary context, requiring that health claims for conventional foods explain the role of the food in the context of the total diet and that such claims be consistent with generally accepted nutritional principles regarding healthy eating. Compare 21 U.S.C. § 343(r)(3)(B)(iii), 343(r)(3)(A)(ii) with 55 Fed. Reg. at 5192. In addition, Congress expressly adopted the same scientific standard of scientific validity for conventional food health claims that FDA had proposed. Compare 21 U.S.C. § 343(r)(3)(B)(i) with 55 Fed. Reg. at 5192. *See* also H. R. Rep. No. 101-538, at 21 (1990) ("House Report"), reprinted in 1990 U.S.C.C.A.N. 3336, 3351. Finally, Congress directed FDA to consider authorizing ten nutrient-disease relationships as health claim topics; six of these had been identified in FDA's 1990 proposal as the health claim topics that the agency intended to first consider authorizing and had been characterized in the proposal as relationships between a nutrient and reduction of the risk of a chronic disease. Compare Pub. L. No. 101-535,

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[4] For example, products formulated to deliver a specified level of glutamine to patients recovering from burns or wounds are medical foods. Burns and other injuries create an increased nutritional need for glutamine, an amino acid.

§ 3(b)(1)(A)(vi), (x), 104 Stat. 2353, 2361 (1990) with 55 Fed. Reg. at 5184. *See* also House Report at 22, reprinted in 1990 U.S.C.C.A.N. at 3352.

The purpose of NLEA was to "clarify and strengthen" FDA's legal authority to permit health claims and require nutrition information in food labeling. House Report at 7, reprinted in 1990 U.S.C.C.A.N. at 3337. The legislative history of the NLEA evidences no Congressional intent to expand the scope of health claims beyond what FDA had envisioned in its 1990 proposal. On the contrary, the legislative history reflects concern that FDA had been too permissive and that health claims in the marketplace needed more control. *See* House Report at 9, reprinted in 1990 U.S.C.C.A.N. at 3338-39.

The legislative history characterizes the health claims that NLEA provides for as claims about preventing or helping to prevent disease. Where examples of health claims are given, they invariably refer to the role of a food substance in preventing or helping to prevent a chronic disease, not to any role in treating an existing disease. *See* House Report at 8, reprinted in 1990 U.S.C.C.A.N. at 3337 ("fiber prevents cancer"); House Report at 20, reprinted in 1990 U.S.C.C.A.N. at 3350 ("fiber helps to prevent cancer"); 136 Cong. Rec. H5841 (statement of intent of changes since bill was reported out of committee) ("fiber prevents cancer"); 136 Cong. Rec. H5841 (statement of Rep. Waxman) ("bran prevents cancer"); 136 Cong. Rec. S16,609 (Statement of Sen. Mitchell) ("reduces the risk of cancer"); 136 Cong. Rec. H12,953 (statement of House floor managers) ("fiber in cereal prevents cancer"); 136 Cong. Rec. H12,954 (statement of Rep. Madigan) ("bran prevents cancer").

The legislative history further indicates that the common purpose behind all three main parts of the NLEA - the nutrition labeling, nutrient content claims, and health claims provisions-was to promote long-term health maintenance and

prevention of disease by providing truthful, scientifically valid information to consumers on the food label. See 136 Cong. Rec. H5843 (statement of Rep. Moakley) (legislation responds to Americans' increasing concern about their diets and reducing the risk of disease); 136 Cong. Rec. H5843 (statement of Rep. Madigan) (question under consideration is how to most effectively inform consumers about health risks related to diet); 136 Cong. Rec. S16,609 (statement of Sen. Metzenbaum) (many Americans use dietary supplements to help prevent chronic disease; rapid scientific advances link nutritional substances to maintenance of long-term health and prevention of long-term disease); 136 Cong. Rec. S16,610-11 (statement of Sen. Hatch) (vitamins and minerals are important in helping to prevent certain serious illnesses and health problems; because of rapid scientific advances linking the prevention of long-term disease to improved nutritional supplementation, important to allow dietary supplements to be marketed so that consumers are informed of the health or disease-prevention benefits they may confer); 136 Cong. Rec. H12,954 (statement of Rep. Moakley) (healthy eating can lower risk for certain illnesses, such as heart disease and cancer). Nowhere in the legislative history are there any statements of Congressional intent to promote the *treatment* of disease with foods.

This general theme that the diet has an important role in reducing the risk, or forestalling the premature onset, of certain chronic disease conditions also was the thrust of the National Research Council's 1989 report entitled "Diet and Health Implications for Reducing Chronic Disease Risk," which provided much of the scientific rationale for health claims, as referenced in FDA's 1990 pre-NLEA proposed rule. *See* 55 Fed. Reg. at 5178. That report clearly focuses on dietary reduction of risk rather than treatment of an existing disease or condition. Similarly, the 1988 Surgeon General's Report on Nutrition and Health focuses on how dietary factors contribute to the development of disease and how

dietary changes can reduce the risk of common chronic diseases, not on how diet can treat disease. That report also was cited in FDA's 1990 proposed rule. *See* 55 Fed. Reg. at 5178. Both reports were cited in the NLEA legislative history, and Congress relied on them in constructing the list of nutrients that must be included in nutrition information on the food label. *See* House Report at 13-14, reprinted in 1990 U.S.C.C.A.N. at 3343. Consequently, there is a significant body of evidence that the 1990 legislation permitting health claims in food labeling was founded on the premise of reducing risk of potential disease, not treatment of existing disease.

We also have considered that the health claim provisions of the NLEA were enacted as part of a statutory scheme that already included extensive, longstanding regulatory requirements for drugs. Before the NLEA, the drug provisions of the FFDCA had been applied to foods, including dietary supplements, that made claims about effects on disease. As discussed in the preceding paragraphs, nothing in the legislative history indicates an intent to abrogate the FFD CA's drug requirements for foods that make disease treatment claims. Moreover, when the Dietary Supplement Health and Education Act of 1994 (DSHEA) was enacted, Congress did not provide that dietary supplements are deemed to be foods in all circumstances; rather, it provided that dietary supplements are deemed to be foods "except for purposes of section 201(g)" of the FFDCA (21 U.S.C. 321(g)), the drug definition. Congress' decision to proceed in this manner, rather than by providing unconditionally that dietary supplements are not drugs, suggests that it wanted the drug provisions to continue to apply to dietary supplements in certain circumstances, such as when the dietary supplement makes a claim about treatment of disease.

We also note that the NLEA specifically exempted medical foods from, among other things, the health claims provisions

that were added to the FFDCA. Pub. L. No. 101-535, § 3(a), 104 Stat. 2353, 2360 (1990) (codified at 21 U.S.C. § 343(r)(5)(A)). *See* also House Report at 22, *reprinted in* 1990 U.S.C.C.A.N. at 3351-52 (noting the exemption). The NLEA was passed just two years after Congress had established medical foods as a new statutory product category for the dietary management of diseases with distinctive nutritional requirements. The exemption from the NLEA health claim provisions for medical foods shows that Congress was aware of the existence of the medical foods category and did not intend an overlap between medical foods and foods bearing health claims. Thus, the statute provides not only clear statutory evidence that claims for dietary management of disease are addressed under the provisions for medical foods, but also clear evidence that Congress intended dietary management claims for foods and health claims for foods to occupy separate regulatory spheres.

C. Agency Interpretation and Application to the Petitioned Claim for Saw Palmetto

FDA has consistently taken the position, in notice and comment rulemaking, that claims to treat disease cannot be made as health claims for foods under the NLEA. As FDA prepared to implement the NLEA, the agency considered the nature of the science supporting dietary effects on disease and Congress' expressed intent to allow conventional foods and dietary supplements to make disease-specific health claims without ceasing to be foods. The agency came to the conclusion that the relationship of a food or food component to a disease is different from that of a drug because of genetic, environmental, dietary and behavioral factors in addition to diet that affect the development of disease, and because of the complexity of foods themselves. 58 Fed. Reg. 2478, 2501-02 (1993). FDA concluded that most types of disease claims that appear on drugs would not be appropriate as health claims on foods because they "imply a degree of

association between the substance and the disease that is not supportable for any food." 56 Fed. Reg. 60537, 60552 (1991). FDA did conclude, however, that science supports some claims that foods can reduce the risk of disease, and that claims of this type are consistent with the statutory differences between foods and drugs.

In preambles to the NLEA health claim regulations, FDA maintained the distinction not only between a health claim target population consisting of the general population (or a subgroup that is at risk for a particular disease) and one consisting of a diseased population, but also between drug claims and food claims. In the January 1994 final rule on health claims for dietary supplements, the agency noted that Congress had given FDA a statutory structure within which to work and that "that structure divides the world of substances that have a relationship to disease into foods and drugs. Congress placed the health claims provisions on the food side of the ledger." 59 Fed. Reg. 395, 411 (1994). In the health claim preambles, we consistently distinguished between nutritional effects of food substances, which we said would be an appropriate subject for a health claim, and effects that are pharmacological, therapeutic, or medicinal, which would not. *See*, e.g., 56 Fed. Reg. at 60545-46; 58 Fed. Reg. at 2501; 59 Fed. Reg. at 408. To the extent the effect of saw palmetto is documented and understood, it is clear that its effect is pharmacological. It is thought to have multiple mechanisms of action on BPH. According to your petition, (page 11; Appendix 2, page 24) the mechanisms most likely involved include inhibition of 5-alpha-reductase, inhibition of binding of dihydrotestosterone to cytosolic androgen recaptors in prostate cells, and alpha-one-adrenergic blocking activity.

In the 1994 final rule, FDA said that claims to "correct an abnormal physiological function caused by a disease or health-related condition" would be drug claims rather than

health claims. 59 Fed. Reg. 395 at 407-08. Your proposed claim for saw palmetto is clearly aimed at correcting an existing abnormal physiological function—namely, urinary abnormalities caused by BPH. With respect to claims about effects on symptoms of disease, the agency said:

> [T]here is no provision in the act for the agency to exempt statements about symptoms of disease from causing products to be regulated as drugs. Although such statements may not be claims that the product will treat the disease that causes the symptoms, the statements clearly pertain to the mitigation of disease by addressing the symptoms caused by the disease. Section 201(g)(1)(B) of the act provides, in part, that articles intended for use in the mitigation of disease are drugs.

59 Fed. Reg. 395 at 413. Your petition clearly identifies the intended use of saw palmetto extract products bearing the proposed claim as the treatment of the urinary symptoms of BPH. The proposed model claim, *"Consumption of 320 mg daily of Saw Palmetto extract may improve urine flow, reduce nocturia and reduce voiding urgency associated with mild benign prostatic hyperplasia (BPH),"* explicitly describes the mitigation of disease by treating its symptoms and establishes the intended use of products bearing the claim as drugs.

With respect to botanicals like saw palmetto, FDA said in a 1993 preamble:

> [T]here is no basis under the act for FDA to permit health claims for herbs whose only known use is for medicinal effects. Health benefits of such herbs may appear in the labeling only in accordance with the drug provisions of the act. . . . Where herbs have a history of use both as foods and drugs, the context of all of the available information on the intended use of the product will determine whether FDA will regulate the herbs as foods, as drugs, or as both foods and drugs.

58 FR at 2501.[5] The history of saw palmetto extract use, as summarized in documents such as the Commission E monograph on saw palmetto berry, the Physicians' Desk Reference for Herbal Medicines, and The Lawrence Review of Natural Products, is solely for medicinal effects in the treatment of urinary symptoms of BPH. The petition includes no information documenting that there is a food use of saw palmetto berries.

D. Further Considerations

Claims about products targeted to persons with a disease invoke a higher level of safety and public health consideration than do claims for products intended for people who, while they may be at risk for a disease, have not yet contracted it. The clear separation of medical foods, and hence intended use for dietary management of disease, from the ordinary food supply with its claims targeted to non-diseased people recognizes that the diseased populations targeted for dietary management are particularly vulnerable by virtue of having the disease. For example, because of this increased vulnerability, the medical foods provision of the Orphan Drug Amendments contemplates supervision by a

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[5] FDA has continued to emphasize the limited scope of health claims in later rulemakings. For example, in 1995, the agency explained, "In contrast to a drug claim, a health claim provides information about how diet can help reduce a person's risk of developing certain diet-related diseases." 60 Fed. Reg. 37502, 37505 (1995). More recently, FDA responded to comments expressing concern that a proposed health claim about oats and coronary heart disease would portray oat products as "magic bullets." The comments argued that the claim would mislead consumers by creating the false impression that consumption of oat bran and oatmeal alone would protect against heart disease. The agency responded that limiting the claim to describing the relationship of a total diet low in saturated fat and cholesterol that includes whole oats to the risk of coronary heart disease would prevent the foods eligible to bear the claim from being perceived as "magic bullets." 62 Fed. Reg. 3584, 3589-90 (1997).

physician to ensure that the medical food is appropriate for the patient and is being used correctly. See 21 U.S.C. § 360ee(b)(3); 61 Fed. Reg. 60661, 60668 (1996). It should also be noted that, consistent with the distinction between foods and drugs articulated by FDA in the health claim preambles, medical foods focus on *dietary* management of disease by meeting distinctive *nutritional* requirements; they do not operate by a pharmacological mechanism.

FDA has considered the use of saw palmetto to treat the symptoms of BPH in the over-the-counter (OTC) drug context. That review concluded that there are health risks associated with the use of saw palmetto to treat BPH symptoms. In a 1990 final rule, FDA concurred with a recommendation from the Advisory Review Panel on OTC Miscellaneous Internal Drug Products that saw palmetto[6] and certain other substances should not be available OTC for the relief of symptoms of BPH. *See* 55 Fed. Reg. 6926 (1990). The agency concluded that the clinical studies testing saw palmetto did not provide "sufficient evidence of effectiveness, i.e., adequate and meaningful clinical improvement" in treating the symptoms of BPH. 55 Fed. Reg. at 6927. Although FDA concluded that saw palmetto "probably" provides some "minimal" symptomatic relief, it expressed concern that, as long as only the symptoms of the condition are relieved, men with BPH may be lulled into a false sense of security and postpone reexamination by a physician, resulting in delay in treatment of the disease. Such delay could result in delayed diagnosis of secondary complications such as stagnation of residual urine, urinary tract infection, and potential renal damage. 55 Fed. Reg. at 6929.

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[6] The final rule refers to saw palmetto as "sabal." Both saw palmetto and sabal are English names for the plant whose Latin binomial name is *Serenoa repens*. *See* 55 Fed. Reg. at 6927.

At FDA's April 4, 2000, public meeting, a physician representing the American Urological Association (AUA) expressed views consistent with those stated in the 1990 final rule. H. Logan Holtgrewe, M.D., emphasized that lower urinary tract symptoms in older men (urinary frequency, urinary urgency, slowing of the urinary stream, hesitation on initiation of urination, getting up several times during the night to urinate) are symptoms of disease, not a normal process of natural aging. Included among the diseases that produce such symptoms are life-threatening cancers, e.g., cancer of the prostate and cancer of the urinary bladder. Dr. Holtgrewe expressed the AUA's concern that men experiencing lower urinary tract symptoms may self-medicate with dietary supplements marketed for such symptoms and thus delay the timely and accurate diagnosis of their cancers. These cancers can rarely be cured once they have spread beyond the confines of the bladder and prostate; a cure is possible only when the disease remains confined to the primary organ. Thus, early diagnosis is essential. Therefore, Dr. Holtgrewe emphasized that dietary supplements marketed for symptoms of BPH may cause "irreparable harm" when men with cancer lose precious time by self-medicating under the illusion that they are treating a benign, non-life-threatening condition. Transcript of Proceedings, "Public Meeting on Implementing the Pearson Court Decision and Other Health Claim Issues," pp. 158-163, 185-205.

E. Consequences of a Contrary Interpretation

Many pharmacologically active substances with possible uses in disease treatment could qualify as dietary ingredients for use in dietary supplements because they are botanicals or otherwise meet the definition of "dietary ingredient" in 21 U.S.C. 321(ff)(1). Likewise, there are a number of substances found in conventional foods that are pharmacologically active. Therefore, if health claims for treatment of disease were permitted, there would be a serious danger that dietary

supplements and food components would undermine the public health protections of the statutory and regulatory requirements for drugs. Approximately 94% of prescription drugs (memorandum from Behrman, May 24, 2000) and almost all OTC drugs for disease uses[7], (memorandum from DeLap, May 26, 2000) are for treatment of disease, rather than disease prevention. Both prescription and OTC drugs are subject to stringent safety and efficacy standards. *See* 21 U.S.C. 321(p), 355(a), (d); 21 C.F.R. Parts 314 and 330. Given the time and expense necessary to bring a new drug to market, it is unlikely that manufacturers would seek drug approval from FDA for any product containing a substance that could be characterized as a dietary supplement or conventional food component, but rather would take the health claim route. For that reason, the protections of the drug approval system and other regulatory requirements applicable to drugs would be lost for a large number of products used to treat disease. Moreover, incentives to perform research would be diminished, since less research is necessary to obtain authorization of a health claim than to meet the new drug approval standard.[8]

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[7] Some OTC drugs are intended for use in affecting the structure or function of the body rather than for use in affecting disease.

[8] Indeed, industry representatives have argued that, under *Pearson v. Shalda*, 164 F.3d 650 (D.C. Cir. 1999), they need only present sufficient evidence to establish that the claim itself is truthful and non-misleading and need not demonstrate that the substance-disease relationship that is the subject of the claim exists. Under this approach, research incentives would be drastically lessened, as a claim could be worded to require minimal research support.

IV. Conclusion

For the reasons discussed above, we are denying your petition.

Sincerely,

/s/ Joseph A. Levitt
JOSEPH A. LEVITT
Director
Center for Food Safety
and Applied Nutrition

REFERENCES

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DeLap, Robert, J. "OTC Drugs for Disease Treatment Uses." FDA Center for Drug Evaluation and Research, Office of Drug Evaluation V, May 26, 2000.

Pearson v. Shalala, 164 F.3d 650 (D.C. Cir. 1999).

APPENDIX D

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT
September Term, 2003
99cv-03247

[Filed March 9, 2004]

No. 03-5020

JULIAN M. WHITAKER, *et al.*,
Appellants,

v.

TOMMY G. THOMPSON, Secretary, U.S. Department of Health and Human Services, et al.,
Appellees.

BEFORE: Ginsburg, *Chief* Judge, Edwards, Sentelle, Henderson, Randolph, Rogers, Tatel, Garland, and Roberts, Circuit Judges, and Williams, *Senior Circuit* Judge.

ORDER

Upon consideration of appellants' petition for rehearing en banc, and the absence of a request by any member of the court for a vote, it is

ORDERED that the petition be denied.

Per Curiam

FOR THE COURT:
Mark J. Langer, Clerk

By: _____
Michael C. McGrail
Deputy Clerk

APPENDIX E

RELEVANT STATUTORY PROVISIONS

1. Section 706(2)(A) of Title 21, United States Code, provides in relevant part:

Scope of review.

To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall—

* * * * *

(2) hold unlawful and set aside agency action, findings, and conclusions found to be

(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law

2. Section 321 of Title 21, United States Code, provides in relevant part:

Definitions; generally

For the purposes of this chapter—

(g)

(1) The term "drug" means

(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and

(B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and

(C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and

(D) articles intended for use as a component of any article specified in clause (A), (B), or (C). A food or dietary supplement for which a claim, subject to sections 343(r)(1)(B) and 343(r)(3) of this title or sections 343(r)(1)(B) and 343(r)(5)(D) of this title, is made in accordance with the requirements of section 343(r) of this title is not a drug solely because the label or the labeling contains such a claim. A food, dietary ingredient, or dietary supplement for which a truthful and not misleading statement is made in accordance with section 343(r)(6) of this title is not a drug under clause (C) solely because the label or the labeling contains such a statement.

(2) The term "counterfeit drug" means a drug which, or the container or labeling of which, without authorization, bears the trademark, trade name, or other identifying mark, imprint, or device, or any likeness thereof, of a drug manufacturer, processor, packer, or distributor other than the person or persons who in fact manufactured, processed, packed, or distributed such drug and which thereby falsely purports or is represented to be the product of, or to have been packed or distributed by, such other drug manufacturer, processor, packer, or distributor.

(m) The term "labeling" means all labels and other written, printed, or graphic matter

(1) upon any article or any of its containers or wrappers, or

(2) accompanying such article.

(ff) The term "dietary supplement"—

(1) means a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients:

(A) a vitamin;

(B) a mineral;

(C) an herb or other botanical;

(D) an amino acid;

(E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or

(F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);

(2) means a product that—

(A)

(i) is intended for ingestion in a form described in section 350(c)(1)(B)(i) of this title; or

(ii) complies with section 350(c)(1)(B)(ii) of this title;

(B) is not represented for use as a conventional food or as a sole item of a meal or the diet; and

(C) is labeled as a dietary supplement; and

(3) does—

(A) include an article that is approved as a new drug under section 355 of this title or licensed as a biologic under section 262 of title 42 and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has issued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages

set forth in the labeling for such dietary supplement, is unlawful under section 342(f) of this title; and

(B) not include—

(i) an article that is approved as a new drug under section 355 of this title, certified as an antibiotic under section 357 of this title, or licensed as a biologic under section 262 of title 42, or

(ii) an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful under this chapter.

Except for purposes of paragraph (g), a dietary supplement shall be deemed to be a food within the meaning of this chapter.

3. Section 343 of Title 21, United States Code, provides in relevant part:

(r) Nutrition levels and health-related claims

(1) Except as provided in clauses (A) through (C) of subparagraph (5), if it is a food intended for human consumption which is offered for sale and for which a claim is made in the label or labeling of the food which expressly or by implication—

* * * * *

(B) characterizes the relationship of any nutrient which is of the type required by paragraph (q)(1) or (q)(2) to be in the label or labeling of the food to a

disease or a health-related condition unless the claim is made in accordance with subparagraph (3) or (5)(D).

* * * * *

(5)

(D) A subparagraph (1)(B) claim made with respect to a dietary supplement of vitamins, minerals, herbs, or other similar nutritional substances shall not be subject to subparagraph (3) but shall be subject to a procedure and standard, respecting the validity of such claim, established by regulation of the Secretary.

* * * * *

(6) For purposes of paragraph (r)(1)(B), a statement for a dietary supplement may be made if—

(A) the statement claims a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, describes the role of a nutrient or dietary ingredient intended to affect the structure or function in humans, characterizes the documented mechanism by which a nutrient or dietary ingredient acts to maintain such structure or function, or describes general well-being from consumption of a nutrient or dietary ingredient,

(B) the manufacturer of the dietary supplement has substantiation that such statement is truthful and not misleading, and

(C) the statement contains, prominently displayed and in boldface type, the following: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." A statement under this subparagraph may not claim to diagnose, mitigate, treat, cure, or prevent a specific disease or

class of diseases. If the manufacturer of a dietary supplement proposes to make a statement described in the first sentence of this subparagraph in the labeling of the dietary supplement, the manufacturer shall notify the Secretary no later than 30 days after the first marketing of the dietary supplement with such statement that such a statement is being made.

4. Section 355 of Title 21, United States Code, provides in relevant part:

New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application

(A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;

(B) a full list of the articles used as components of such drug;

(C) a full statement of the composition of such drug;

(D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;

(E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and

(F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).

* * * * *

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

* * * * *

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection

(b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984, and if the holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:

* * * * *

(D)

(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including

any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for ad drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification

of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after Sep-

tember 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailabilty [sic] studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

APPENDIX F

TITLE 21—FOOD AND DRUGS

CHAPTER I—FOOD AND DRUG ADMINISTRATION DEPARTMENT OF HEALTH AND HUMAN SERVICES

PART 101—FOOD LABELING

Subpart A—General Provisions

Sec. 101.14 Health claims: general requirements.

(a) Definitions. For purposes of this section, the following definitions apply:

(1) Health claim means any claim made on the label or in labeling of a food, including a dietary supplement, that expressly or by implication, including "third party" references, written statements (e.g., a brand name including a term such as "heart"), symbols (e.g., a heart symbol), or vignettes, characterizes the relationship of any substance to a disease or health-related condition. Implied health claims include those statements, symbols, vignettes, or other forms of communication that suggest, within the context in which they are presented, that a relationship exists between the presence or level of a substance in the food and a disease or health-related condition.

(2) Substance means a specific food or component of food, regardless of whether the food is in conventional food form or a dietary supplement that includes vitamins, minerals, herbs, or other similar nutritional substances.

(3) Nutritive value means a value in sustaining human existence by such processes as promoting growth, replacing loss of essential nutrients, or providing energy.

(4) Disqualifying nutrient levels means the levels of total fat, saturated fat, cholesterol, or sodium in a food above which the food will be disqualified from making a health claim. These levels are 13.0 grams (g) of fat, 4.0 g of

saturated fat, 60 milligrams (mg) of cholesterol, or 480 mg of sodium, per reference amount customarily consumed, per label serving size, and, only for foods with reference amounts customarily consumed of 30 g or less or 2 tablespoons or less, per 50 g. For dehydrated foods that must have water added to them prior to typical consumption, the per 50g criterion refers to the as prepared form. Any one of the levels, on a per reference amount customarily consumed, a per label serving size or, when applicable, a per 50 g basis, will disqualify a food from making a health claim unless an exception is provided in subpart E of this part, except that:

(i) The levels for a meal product as defined in Sec. 101.13(l) are 26.0 g of fat, 8.0 g of saturated fat, 120 mg of cholesterol, or 960 mg of sodium per label serving size, and

(ii) The levels for a main dish product as defined in Sec. 101.13(m) are 19.5 g of fat, 6.0 g of saturated fat, 90 mg of cholesterol, or 720 mg of sodium per label serving size.

(5) Disease or health-related condition means damage to an organ, part, structure, or system of the body such that it does not function properly (e.g., cardiovascular disease), or a state of health leading to such dysfunctioning (e.g., hypertension); except that diseases resulting from essential nutrient deficiencies (e.g., scurvy, pellagra) are not included in this definition (claims pertaining to such diseases are thereby not subject to Sec. 101.14 or Sec. 101.70).

(b) Eligibility. For a substance to be eligible for a health claim:

(1) The substance must be associated with a disease or health-related condition for which the general U.S. population, or an identified U.S. population subgroup (e.g., the elderly) is at risk, or, alternatively, the petition submitted by the proponent of the claim otherwise explains the prevalence

of the disease or health-related condition in the U.S. population and the relevance of the claim in the context of the total daily diet and satisfies the other requirements of this section.

(2) If the substance is to be consumed as a component of a conventional food at decreased dietary levels, the substance must be a nutrient listed in 21 U.S.C. 343(q)(1)(C) or (q)(1)(D), or one that the Food and Drug Administration (FDA) has required to be included in the label or labeling under 21 U.S.C. 343(q)(2)(A); or

(3) If the substance is to be consumed at other than decreased dietary levels:

(i) The substance must, regardless of whether the food is a conventional food or a dietary supplement, contribute taste, aroma, or nutritive value, or any other technical effect listed in Sec. 170.3(o) of this chapter, to the food and must retain that attribute when consumed at levels that are necessary to justify a claim; and

(ii) The substance must be a food or a food ingredient or a component of a food ingredient whose use at the levels necessary to justify a claim has been demonstrated by the proponent of the claim, to FDA's satisfaction, to be safe and lawful under the applicable food safety provisions of the Federal Food, Drug, and Cosmetic Act.

(c) Validity requirement. FDA will promulgate regulations authorizing a health claim only when it determines, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), that there is significant scientific agreement, among experts qualified by scientific training and

experience to evaluate such claims, that the claim is supported by such evidence.

(d) General health claim labeling requirements. (1) When FDA determines that a health claim meets the validity requirements of paragraph (c) of this section, FDA will propose a regulation in subpart E of this part to authorize the use of that claim. If the claim pertains to a substance not provided for in Sec. 101.9 or Sec. 101.36, FDA will propose amending that regulation to include declaration of the substance.

(2) When FDA has adopted a regulation in subpart E of this part providing for a health claim, firms may make claims based on the regulation in subpart E of this part, provided that:

(i) All label or labeling statements about the substance-disease relationship that is the subject of the claim are based on, and consistent with, the conclusions set forth in the regulations in subpart E of this part;

(ii) The claim is limited to describing the value that ingestion (or reduced ingestion) of the substance, as part of a total dietary pattern, may have on a particular disease or health-related condition;

(iii) The claim is complete, truthful, and not misleading. Where factors other than dietary intake of the substance affect the relationship between the substance and the disease or health-related condition, such factors may be required to be addressed in the claim by a specific regulation in subpart E of this part;

(iv) All information required to be included in the claim appears in one place without other intervening material, except that the principal display panel of the label or labeling may bear

the reference statement, "See —— for information about the relationship between —— and ——," with the blanks filled in with the location of the labeling containing the health claim, the name of the substance, and the disease or health-related condition (e.g., "See attached pamphlet for information about calcium and osteoporosis"), with the entire claim appearing elsewhere on the other labeling, provided that, where any graphic material (e.g., a heart symbol) constituting an explicit or implied health claim appears on the label or labeling, the reference statement or the complete claim shall appear in immediate proximity to such graphic material;

(v) The claim enables the public to comprehend the information provided and to understand the relative significance of such information in the context of a total daily diet; and

(vi) If the claim is about the effects of consuming the substance at decreased dietary levels, the level of the substance in the food is sufficiently low to justify the claim. To meet this requirement, if a definition for use of the term low has been established for that substance under this part, the substance must be present at a level that meets the requirements for use of that term, unless a specific alternative level has been established for the substance in subpart E of this part. If no definition for "low" has been established, the level of the substance must meet the level established in the regulation authorizing the claim; or

(vii) If the claim is about the effects of consuming the substance at other than decreased dietary levels, the level of the substance is sufficiently high and

in an appropriate form to justify the claim. To meet this requirement, if a definition for use of the term high for that substance has been established under this part, the substance must be present at a level that meets the requirements for use of that term, unless a specific alternative level has been established for the substance in subpart E of this part. If no definition for "high" has been established (e.g., where the claim pertains to a food either as a whole food or as an ingredient in another food), the claim must specify the daily dietary intake necessary to achieve the claimed effect, as established in the regulation authorizing the claim; Provided That:

(A) Where the food that bears the claim meets the requirements of paragraphs (d)(2)(vi) or (d)(2)(vii) of this section based on its reference amount customarily consumed, and the labeled serving size differs from that amount, the claim shall be followed by a statement explaining that the claim is based on the reference amount rather than the labeled serving size (e.g., "Diets low in sodium may reduce the risk of high blood pressure, a disease associated with many factors. A serving of—ounces of this product conforms to such a diet.").

(B) Where the food that bears the claim is sold in a restaurant or in other establishments in which food that is ready for immediate human consumption is sold, the food can meet the requirements of paragraphs (d)(2)(vi) or (d)(2)(vii) of this section if the firm that sells the food has a reasonable basis on which to believe that the food that bears the claim meets the requirements of paragraphs (d)(2)(vi) or (d)(2)(vii) of this section and provides that basis upon request.

(3) Nutrition labeling shall be provided in the label or labeling of any food for which a health claim is made in accordance with Sec. 101.9; for restaurant foods, in accord-

ance with Sec. 101.10; or for dietary supplements, in accordance with Sec. 101.36.

(e) Prohibited health claims. No expressed or implied health claim may be made on the label or in labeling for a food regardless of whether the food is in conventional food form or dietary supplement form, unless:

(1) The claim is specifically provided for in subpart E of this part; and

(2) The claim conforms to all general provisions of this section as well as to all specific provisions in the appropriate section of subpart E of this part;

(3) None of the disqualifying levels identified in paragraph (a)(4) of this section is exceeded in the food, unless specific alternative levels have been established for the substance in subpart E of this part; or unless FDA has permitted a claim despite the fact that a disqualifying level of a nutrient is present in the food based on a finding that such a claim will assist consumers in maintaining healthy dietary practices, and, in accordance with the regulation in subpart E of this part that makes such a finding, the label bears a disclosure statement that complies with Sec. 101.13(h), highlighting the nutrient that exceeds the disqualifying level;

(4) Except as provided in paragraph (e)(3) of this section, no substance is present at an inappropriate level as determined in the specific provision authorizing the claim in subpart E of this part;

(5) The label does not represent or purport that the food is for infants and toddlers less than 2 years of age except if the claim is specifically provided for in subpart E of this part; and

(6) Except for dietary supplements or where provided for in other regulations in part 101, subpart E, the food contains 10 percent or more of the Reference Daily Intake or the Daily

Reference Value for vitamin A, vitamin C, iron, calcium, protein, or fiber per reference amount customarily consumed prior to any nutrient addition.

(f) The requirements of this section do not apply to:

(1) Infant formulas subject to section 412(h) of the Federal Food, Drug, and Cosmetic Act, and

(2) Medical foods defined by section 5(b) of the Orphan Drug Act.

(g) Applicability. The requirements of this section apply to foods intended for human consumption that are offered for sale, regardless of whether the foods are in conventional food form or dietary supplement form.

Subpart E—Specific Requirements for Health Claims

Sec. 101.70 Petitions for health claims.

(a) Any interested person may petition the Food and Drug Administration (FDA) to issue a regulation regarding a health claim. An original and one copy of the petition shall be submitted, or the petitioner may submit an original and a computer readable disk containing the petition. Contents of the disk should be in a standard format, such as ASCII format. (Petitioners interested in submitting a disk should contact the Center for Food Safety and Applied Nutrition for details.) If any part of the material submitted is in a foreign language, it shall be accompanied by an accurate and complete English translation. The petition shall state the petitioner's post office address to which any correspondence required by section 403 of the Federal Food, Drug, and Cosmetic Act may be sent.

(b) Pertinent information may be incorporated in, and will be considered as part of, a petition on the basis of specific reference to such information submitted to and retained in the files of FDA. Such information may include any findings, along with the basis of the findings, of an outside panel with

expertise in the subject area. Any reference to published information shall be accompanied by reprints, or easily readable copies of such information.

(c) If nonclinical laboratory studies are included in a petition, the petition shall include, with respect to each nonclinical study contained in the petition, either a statement that the study has been conducted in compliance with the good laboratory practice regulations as set forth in part 58 of this chapter, or, if any such study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance.

(d) If clinical or other human investigations are included in a petition, the petition shall include a statement that they were either conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter, or were not subject to such requirements in accordance with Sec. 56.104 or Sec. 56.105, and a statement that they were conducted in compliance with the requirements for informed consent set forth in part 50 of this chapter.

(e) All data and information in a health claim petition are available for public disclosure after the notice of filing of petition is issued to the petitioner, except that clinical investigation reports, adverse reaction reports, product experience reports, consumer complaints, and other similar data and information shall only be available after deletion of:

(1) Names and any information that would identify the person using the product.

(2) Names and any information that would identify any third party involved with the report, such as a physician or hospital or other institution.

(f) Petitions for a health claim shall include the following data and be submitted in the following form:

(Date)_____

Name of petitioner _____

Post office address _____

Subject of the petition _____

Food and Drug Administration,

Office of Nutritional Products, Labeling and Dietary Supplements (HFS-800),

5100 Paint Branch Pkwy.,

College Park, MD 20740,

The undersigned, _____ submits this petition pursuant to section 403(r)(4) or 403(r)(5)(D) of the Federal Food, Drug, and Cosmetic Act with respect to (statement of the substance and its health claim).

Attached hereto, and constituting a part of this petition, are the following:

A. Preliminary requirements. A complete explanation of how the substance conforms to the requirements of Sec. 101.14(b) (21 CFR 101.14(b)). For petitions where the subject substance is a food ingredient or a component of a food ingredient, the petitioner should compile a comprehensive list of the specific ingredients that will be added to the food to supply the substance in the food bearing the health claim. For each such ingredient listed, the petitioner should state how the ingredient complies with the requirements of Sec. 101.14(b)(3)(ii), e.g., that its use is generally recognized as safe (GRAS), listed as a food additive, or authorized by a prior sanction issued by the agency, and what the basis is for the GRAS claim, the food additive status, or prior sanctioned status.

B. Summary of scientific data. The summary of scientific data provides the basis upon which authorizing a health claim can be justified as providing the health benefit. The summary must establish that, based on the totality of publicly available scientific evidence (including evidence from well-designed studies conducted in a manner which is consistent with generally recognized scientific procedures and principles), there is significant scientific agreement among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by such evidence.

The summary shall state what public health benefit will derive from use of the claim as proposed. If the claim is intended for a specific group within the population, the summary shall specifically address nutritional needs of such group and shall include scientific data showing how the claim is likely to assist in meeting such needs.

The summary shall concentrate on the findings of appropriate review articles, National Institutes of Health consensus development conferences, and other appropriate resource materials. Issues addressed in the summary shall include answers to such questions as:

1. Is there an optimum level of the particular substance to be consumed beyond which no benefit would be expected?

2. Is there any level at which an adverse effect from the substance or from foods containing the substance occurs for any segment of the population?

3. Are there certain populations that must receive special consideration?

4. What other nutritional or health factors (both positive and negative) are important to consider when consuming the substance?

In addition, the summary of scientific data shall include a detailed analysis of the potential effect of the use of the

proposed claim on food consumption, specifically any change due to significant alterations in eating habits and corresponding changes in nutrient intake resulting from such changes in food consumption. The latter item shall specifically address the effect on the intake of nutrients that have beneficial and negative consequences in the total diet.

If the claim is intended for a significant subpopulation within the general U.S. population, the analysis shall specifically address the dietary practices of such group, and shall include data sufficient to demonstrate that the dietary analysis is representative of such group (e.g., adolescents or the elderly).

If appropriate, the petition shall explain the prevalence of the disease or health-related condition in the U.S. population and the relevance of the claim in the context of the total daily diet.

Also, the summary shall demonstrate that the substance that is the subject of the proposed claim conforms to the definition of the term "substance" in Sec. 101.14(a)(2).

C. Analytical data that show the amount of the substance that is present in representative foods that would be candidates to bear the claim should be obtained from representative samples using methods from the Association of Official Analytical Chemists (AOAC), where available. If no AOAC method is available, the petitioner shall submit the assay method used and data establishing the validity of the method for assaying the substance in food. The validation data should include a statistical analysis of the analytical and product variability.

D. Model health claim. One or more model health claims that represent label statements that may be used on a food label or in labeling for a food to characterize the relationship between the substance in a food to a disease or health-related condition that is justified by the summary of scientific data

provided in section C of the petition. The model health claim shall include:

1. A brief capsulized statement of the relevant conclusions of the summary, and

2. A statement of how this substance helps the consumer to attain a total dietary pattern or goal associated with the health benefit that is provided.

E. The petition shall include the following attachments:

1. Copies of any computer literature searches done by the petitioner (e.g., Medline).

2. Copies of articles cited in the literature searches and other information as follows:

a. All information relied upon for the support of the health claim, including copies of publications or other information cited in review articles and used to perform meta-analyses.

b. All information concerning adverse consequences to any segment of the population (e.g., sensitivity to the substance).

c. All information pertaining to the U.S. population.

F. The petitioner is required to submit either a claim for categorical exclusion under Sec. 25.30 or Sec. 25.32 of this chapter or an environmental assessment under Sec. 25.40 of this chapter.

Yours very truly,

Petitioner _____

By _____

(Indicate authority)

(g) The data specified under the several lettered headings should be submitted on separate pages or sets of pages, suitably identified. If such data have already been submitted

with an earlier application from the petitioner or any other final petition, the present petition may incorporate it by specific reference to the earlier petition.

(h) The petition shall include a statement signed by the person responsible for the petition that, to the best of his/her knowledge, it is a representative and balanced submission that includes unfavorable information as well as favorable information, known to him/her to be pertinent to the evaluation of the proposed health claim.

(i) The petition shall be signed by the petitioner or by his/her attorney or agent, or (if a corporation) by an authorized official.

(j) Agency action on the petition. (1) Within 15 days of receipt of the petition, the petitioner will be notified by letter of the date on which the petition was received. Such notice will inform the petitioner that the petition is undergoing agency review and that the petitioner will subsequently be notified of the agency's decision to file for comprehensive review or deny the petition.

(2) Within 100 days of the date of receipt of the petition, FDA will notify the petitioner by letter that the petition has either been filed for comprehensive review or denied. The agency will deny a petition without reviewing the information contained in "B. Summary of Scientific Data" if the information in "A. Preliminary Requirements" is inadequate in explaining how the substance conforms to the requirements of Sec. 101.14(b). If the petition is denied, the notification will state the reasons therefor, including justification of the rejection of any report from an authoritative scientific body of the U.S. Government. If filed, the date of the notification letter becomes the date of filing for the purposes of this regulation. If FDA does not act within such 100 days, the petition shall be deemed to be denied unless an extension is mutually agreed upon by FDA and the petitioner. A petition

that has been denied, or has been deemed to be denied, without filing will not be made available to the public. A filed petition will be available to the public to the extent provided under paragraph (e) of this section.

(3) Within 90 days of the date of filing, FDA will by letter of notification to the petitioner:

(i) Deny the petition, or

(ii) Inform the petitioner that a proposed regulation to provide for the requested use of the health claim will be published in the Federal Register. If the petition is denied, the notification will state the reasons therefor, including justification for the rejection of any report from an authoritative scientific body of the U.S. Government. FDA will publish the proposal to amend the regulations to provide for the requested use of the health claim in the Federal Register within 90 days of the date of filing. The proposal will also announce the availability of the petition for public review.

(iii) If FDA does not act within 90 days of the date of filing, the petition shall be deemed to be denied unless an extension is mutually agreed upon by FDA and the petitioner.

(4)(i) Within 270 days of the date of publication of the proposal, FDA will publish a final rule that either authorizes use of the health claim or explains why the agency has decided not to authorize one.

(ii) For cause, FDA may extend, no more than twice, the period in which it will publish a final rule; each such extension will be for no more than 90 days. FDA will publish a notice of each extension in the Federal Register. The document will state the basis for the extension, the length of the extension, and the date by which the final rule will be published, which date

shall be within 540 days of the date of receipt of the petition.

Sec. 101.75 Health claims: dietary saturated fat and cholesterol and risk of coronary heart disease.

(a) Relationship between dietary saturated fat and cholesterol and risk of coronary heart disease. (1) Cardiovascular disease means diseases of the heart and circulatory system. Coronary heart disease is the most common and serious form of cardiovascular disease and refers to diseases of the heart muscle and supporting blood vessels. High blood total- and low density lipoprotein (LDL)-cholesterol levels are major modifiable risk factors in the development of coronary heart disease. High coronary heart disease rates occur among people with high blood cholesterol levels of 240 milligrams/decaliter (mg/dL) (6.21 millimoles per liter (mmol/L)) or above and LDL-cholesterol levels of 160 mg/dL (4.13 mmol/L) or above. Borderline high risk blood cholesterol levels range from 200 to 239 mg/dL (5.17 to 6.18 mmol/L) and 130 to 159 mg/dL (3.36 to 4.11 mmol/L) of LDL-cholesterol. Dietary lipids (fats) include fatty acids and cholesterol. Total fat, commonly referred to as fat, is composed of saturated fat (fatty acids containing no double bonds), and monounsaturated and polyunsaturated fat (fatty acids containing one or more double bonds).

(2) The scientific evidence establishes that diets high in saturated fat and cholesterol are associated with increased levels of blood total-and LDL-cholesterol and, thus, with increased risk of coronary heart disease. Diets low in saturated fat and cholesterol are associated with decreased levels of blood total-and LDL-cholesterol, and thus, with decreased risk of developing coronary heart disease.

(b) Significance of the relationship between dietary saturated fat and cholesterol and risk of coronary heart disease. (1) Coronary heart disease is a major public health

concern in the United States, primarily because it accounts for more deaths than any other disease or group of diseases. Early management of risk factors for coronary heart disease is a major public health goal that can assist in reducing risk of coronary heart disease. There is a continuum of mortality risk from coronary heart disease that increases with increasing levels of blood LDL-cholesterol. Individuals with high blood LDL-cholesterol are at greatest risk. A larger number of individuals with more moderately elevated cholesterol also have increased risk of coronary events; such individuals comprise a substantial proportion of the adult U.S. population. The scientific evidence indicates that reducing saturated fat and cholesterol intakes lowers blood LDL-cholesterol and risk of heart disease in most individuals. There is also evidence that reducing saturated fat and cholesterol intakes in persons with blood cholesterol levels in the normal range also reduces risk of heart disease.

(2) Other risk factors for coronary heart disease include a family history of heart disease, high blood pressure, diabetes, cigarette smoking, obesity (body weight 30 percent greater than ideal body weight), and lack of regular physical exercise.

(3) Intakes of saturated fat exceed recommended levels in many people in the United States. Intakes of cholesterol are, on average, at or above recommended levels. One of the major public health recommendations relative to coronary heart disease risk is to consume less than 10 percent of calories from saturated fat, and an average of 30 percent or less of total calories from all fat. Recommended daily cholesterol intakes are 300 mg or less per day.

(c) Requirements. (1) All requirements set forth in Sec. 101.14 shall be met.

(2) Specific requirements—(i) Nature of the claim. A health claim associating diets low in saturated fat and

cholesterol with reduced risk of coronary heart disease may be made on the label or labeling of a food described in paragraph (c)(2)(ii) of this section provided that:

(A) The claim states that diets low in saturated fat and cholesterol "may" or "might" reduce the risk of heart disease;

(B) In specifying the disease, the claim uses the terms "heart disease" or "coronary heart disease;"

(C) In specifying the nutrient, the claim uses the terms "saturated fat" and "cholesterol" and lists both;

(D) The claim does not attribute any degree of risk reduction for coronary heart disease to diets low in dietary saturated fat and cholesterol; and

(E) The claim states that coronary heart disease risk depends on many factors.

(ii) Nature of the food. The food shall meet all of the nutrient content requirements of Sec. 101.62 for a "low saturated fat," "low cholesterol," and "low fat" food; except that fish and game meats (i.e., deer, bison, rabbit, quail, wild turkey, geese, and ostrich) may meet the requirements for "extra lean" in Sec. 101.62.

(d) Optional information. (1) The claim may identify one or more of the following risk factors in addition to saturated fat and cholesterol about which there is general scientific agreement that they are major risk factors for this disease: A family history of coronary heart disease, elevated blood total and LDL-cholesterol, excess body weight, high blood pressure, cigarette smoking, diabetes, and physical inactivity.

(2) The claim may indicate that the relationship of saturated fat and cholesterol to heart disease is through the intermediate link of "blood cholesterol" or "blood total- and LDL cholesterol."

(3) The claim may include information from paragraphs (a) and (b) of this section, which summarize the relationship between dietary saturated fat and cholesterol and risk of coronary heart disease, and the significance of the relationship.

(4) In specifying the nutrients, the claim may include the term "total fat" in addition to the terms "saturated fat" and "cholesterol".

(5) The claim may include information on the number of people in the United States who have coronary heart disease. The sources of this information shall be identified, and it shall be current information from the National Center for Health Statistics, the National Institutes of Health, or "Nutrition and Your Health: Dietary Guidelines for Americans," U.S. Department of Health and Human Services (DHHS) and U.S. Department of Agriculture (USDA), Government Printing Office.

(6) The claim may indicate that it is consistent with "Nutrition and Your Health: Dietary Guidelines for Americans," DHHS and USDA, Government Printing Office.

(7) The claim may state that individuals with elevated blood total-or LDL-cholesterol should consult their physiccians for medical advice and treatment. If the claim defines high or normal blood total-or LDL-cholesterol levels, then the claim shall state that individuals with high blood cholesterol should consult their physicians for medical advice and treatment.

(e) Model health claims.The following are model health claims that may be used in food labeling to describe the relationship between dietary saturated fat and cholesterol and risk of heart disease:

(1) While many factors affect heart disease, diets low in saturated fat and cholesterol may reduce the risk of this disease;

(2) Development of heart disease depends upon many factors, but its risk may be reduced by diets low in saturated fat and cholesterol and healthy lifestyles;

(3) Development of heart disease depends upon many factors, including a family history of the disease, high blood LDL-cholesterol, diabetes, high blood pressure, being overweight, cigarette smoking, lack of exercise, and the type of dietary pattern. A healthful diet low in saturated fat, total fat, and cholesterol, as part of a healthy lifestyle, may lower blood cholesterol levels and may reduce the risk of heart disease;

(4) Many factors, such as a family history of the disease, increased blood-and LDL-cholesterol levels, high blood pressure, cigarette smoking, diabetes, and being overweight, contribute to developing heart disease. A diet low in saturated fat, cholesterol, and total fat may help reduce the risk of heart disease; and

(5) Diets low in saturated fat, cholesterol, and total fat may reduce the risk of heart disease. Heart disease is dependent upon many factors, including diet, a family history of the disease, elevated blood LDL-cholesterol levels, and physical inactivity.

APPENDIX G

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Washington, DC 20204

December 1, 1999

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1050 Seventeenth Street, NW
Suite 600
Washington, DC 20036

RE: Petition for Health Claim: Saw Palmetto and Benign Prostatic Hyperplasia (Docket Number 99P-3030)

Dear Mr. Emord:

This responds to you health claim petition dated May 25, 1999, submitted to the Food and Drug Administration (FDA) on behalf of Julian Whitaker, M.D., Durk Pearson and Sandy Shaw, American Preventive Medical Association, and Pure Encapsulations, Inc., requesting that the agency authorize a health claim on the relationship between dietary supplements of saw palmetto extract (specifically the *n*-hexane lipido-sterolic extract of the pulp and seed of the dwarf American palm, *Serona repens*) and benign prostatic hyperplasia. Your petition was filed for comprehensive review on September 1, 1999, in accord with the procedures in 21 CFR § 101.70(j)(2). Ninety days have passed since the petition was filed and FDA has not taken action to deny the petition or to publish a proposed regulation to provide for the requested use of the health claim; thus, the petition is deemed to be denied under 21 U.S.C. § 343(r)(4)(A)(i) and 21 CFR § 101.70(j)(3)(iii).

FDA has allowed your petition to be denied by operation of law because the agency has been unable to resolve an important and novel issue that the petition raised. All previous

health claim petitions that met the eligibility requirements in 21 CFR § 101.14(b) have addressed reduction of the risk of a disease or health-related condition. Because your petition goes beyond risk reduction to claim an effect on an existing disease, the agency has had to consider seriously whether health claims for foods (including dietary supplements) may encompass this type of claim or whether such a claim is appropriate only on a product that has been shown to meet the safety and efficacy requirements for drugs. The agency has been unable to reach a decision on your petition within the time provided by statute and regulation, and has decided to seek public input on the important question it raised. We will continue to work diligently to resolve this issue and, when a resolution is achieved, the agency will, on its own initiative, reconsider your health claim petition.

We will communicate with you shortly to advise you further regarding the procedure and process that we will use to make our decision.

Sincerely,

/s/ Elizabeth A. Yetley
ELIZABETH A. YETLEY, Ph.D.
Office of Special Nutritionals
Center for Food Safety and Applied Nutrition